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A CANCER DETECTION SURVEY OF CARCINOMA OF THE LUNG AND FEMALE PELVIS AMONG NAVAJOS ON THE NAVAJO INDIAN RESERVATION

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NAVAJO, or the Anglicized word "Navaho," is a corruption of the Pueblo Indian word "Nava-hu", which means "The People." In their own Athabascan language, the Navajo refer to themselves as "din-eh," which also means "The People." The Spaniards adopted the term Navajo from the Pueblo Indians and it has been used ever since.

The Navajos are a remarkable people in many ways. They with the Apaches represent the southernmost mass penetration of Indians of the Athabascan ethnographic system. They are archeologically unaccounted for earlier than the fourteenth century. They were persecuted by the Spanish and subsequently by the Mexicans as marauders, and were later regarded as such by the United States government after its acquisition of the area now comprising Arizona and New Mexico. In 1864 they were gathered by United States government soldiers under the command of Colonel Kit Carson, their herds killed, and their field crops and orchards destroyed. In many instances those who resisted the regimentation, both warriors and civilians, were killed. Most of the remaining population was moved from the high plateaus to the lowlands of the Rio Grande valley, Fort Sumner. Many died on the circuitous foot march of several hundred miles, only 25,000 or less arriving at the destination. After 4 years of trying, without success, to make farmers of the group, the government returned them to their own lands, a remnant of 7,500 individuals. Eighty-nine years later, in 1957, despite drought, high infant mortality, high maternal mortality, widespread childhood disease, tuberculosis, and all the other ills and plagues which have beset Indians in the United States, the Navajos have increased until they are the most numerous tribe of

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American Indians, more than 80,000 according to latest population estimates. The United States Public Health Service states that their population growth amounts to more than 2½ per cent annually.

The population is scattered over 25,000 square miles of reservation in Arizona, New Mexico, Utah, and Colorado, living in small family groups. On reservation they support themselves principally as herdsmen, handcraftsmen, miners, and in varied governmental positions. Off reservation employment is more varied though many are engaged in season as farm laborers and railroad workers. They are an intelligent people, highly individualistic, hardy, handsome, and athletic. They adapt easily to economic and social change.

Among the Navajos, the grazing herds are walking larders with the lambs, wool, and pelts offered for sale or barter. Sheep and goats are slaughtered for food as needed. The slaughtered animal is used *in toto*, including the viscera, the more rapidly autolizing parts being prepared and consumed soon after sacrifice of the animal, and the muscle parts conserved for later use. Each family generally has a garden of corn, squash, beans, and melons. Occasionally peaches are grown in the canyons. The garden and orchard produce is for human rather than animal consumption. Food is prepared for each meal as needed—usually as a stew or by roasting over wood coals.

Dress of the men is comparable to that in the rural western states, while the women usually wear very fully pleated skirts, ankle length, and secured at the waist by a safety pin. The "Navajo shirt" is standard covering for the women. Quite ornate jewelry of silver and turquoise, and plenty of it, is the rule in the form of bracelets, necklaces, and earrings for both men and women.

An unusual facet of the Navajo people is their deficit in malignant disease morbidity and mortality. Salsbury found no case of carcinoma of the female breast in over 34,500 admissions at the Sage Memorial Hospital, Ganado, Arizona, although several in the white population of the sponsoring mission and nearby traders' families were operated upon during this period. Collecting the statistics of 60,000 hospital admissions to the United States government and mission hospitals on the Navajo reservation, he found but 3 cases of carcinoma of the breast in Navajo women. Another deviation found was in the relative morbidity in pelvic cancer. Although 38 carcinomas of the cervix were found in the survey, there was but 1 carcinoma of the endometrium. This ratio of 1 in 38, although not believed to be sound, still varies greatly from the relative frequency quoted in Novak and Novak as being 1 to 3. Only 1 case of carcinoma of the "ovary, tube, or broad ligament" was reported, and no carcinoma of the penis was named as such, although the Navajos are not as a rule circumcised.

Smith (8) and Smith, Salsbury, and Giliam (9) have reported on the rate of malignant disease in the Indians in general and in the Navajo specifically. In the last mentioned study, the death certificates at the Window Rock Agency for the years 1948 to 1952 were searched. Seven cases of carcinoma of the cervix were found, and but 1 "malignant neoplasm, uterus, unspecified." Smith, Salsbury, and Giliam concluded that there is indeed a deficit of malignant disease as a whole, and more specifically of the female breast, pelvis, the male prostate, and the lung in the Navajo. Smith concluded that a similar situation exists in American Indians in general.

It was the 23 years' observation by one of us (Salsbury) as surgeon to the Sage Memorial Hospital, Ganado, Arizona, of the low incidence of cancer in the Navajo which led to the present expeditions to the Navajo, of which this is the fourth sponsored by the Arizona State Health Department. After it was established that there is indeed a deficit of malignant disease among the Navajos, Darby and associates studied the nutritional aspects of the Navajo regimen with reference to their nutriture, finding only 1 case of pellagra in 1,200 individuals examined. A

low level of serum ascorbic acid reflected the low intake of vitamin C. The general health seemed to be equivalent to that of similar groups. Pertaining to malignant disease, Darby concluded that with our present knowledge no likely difference in the nutriture is present which would explain the low rate of malignant disease in the Navajo tribe. He hypothesizes that a genetic influence rather than a dietary influence is the more logical explanation, as in the reported low incidence of carcinoma of the cervix in Jewish women.

The present study was made with the purpose of clinically sampling the population as fully as possible, screening for carcinoma in general, with emphasis on carcinoma of the lung and female pelvis.

Professional personnel were recruited almost entirely among individuals closely associated with the principal researchers and under the general supervision of Clarence G. Salsbury, M.D., Commissioner, Arizona State Department of Health. Business management was delegated to Miss Elma R. Smith. Clerical and other subsidiary staff were recruited among Arizona residents, using Indians wherever possible. The group was divided into two teams, each consisting of two physicians, a laboratory technician, a radiologic technician, a Navajo nurse, a Navajo clerk-typist, and a Navajo truck driver. General project headquarters were established at Ganado, Arizona, together with one research team. The other team was set up for operation at Pinon, Arizona.

Locations were selected because they had previously been used by the Darby teams and represented the accessible and the remote portions of the population. Ganado, Arizona, is the site of a Presbyterian church mission and has had medical facilities almost from the date of its founding in 1901, while Pinon, Arizona, has only the full time services of a public health nurse and the occasional mobile clinic services offered by the United States Public Health Service. Ganado is served by a paved highway to Gallup, New Mexico, 56 miles away; Pinon, on the other hand, is 125 miles from the nearest railroad and 26 miles from the nearest paved road. Transportation at Ganado is preponderantly by pickup truck whereas at Pinon the horse or one's own leg power is the most frequent mode of transportation. Among the Navajos, life at Pinon is more like what it was 50 years ago.

TABLE I.—ESTIMATED ARIZONA NAVAJO POPULATION BY AGE GROUP AND SEX (MIDYEAR, 1957)

Age group, years	*Total No.*	*No. of males*	*No. of females*
Total	50,425	25,082	25,343
0– 4	8,868	4,496	4,372
5– 9	8,066	4,005	4,061
10–14	6,344	3,285	3,059
15–19	5,444	2,579	2,865
Total under 20	28,722	14,365	14,357
20–24	4,601	2,182	2,419
25–29	3,265	1,573	1,692
30–34	2,573	1,205	1,368
35–39	2,342	1,128	1,214
40–44	1,888	903	985
45–49	1,777	905	872
50–54	1,261	675	586
55–59	1,055	593	462
60–64	846	453	393
65–69	797	423	374
70–74	520	268	252
75 and over	778	409	369
Total over 20	21,703	10,717	10,986

Estimated by percentage distribution from population reports of Bureau of Indian Affairs, Navajo Agency, Window Rock, Arizona, Program Analysis, July 1957.

Prior to any detailed planning, permission to conduct the project was given to the Arizona State Department of Health by the Navajo Tribal Council. When the plans were completed, the Indians were advised of the program by the Tribal Council, by the public and mission school administrations, and by Mrs. Annie Wauneka through her Navajo language radio broadcasts. The examinations were begun in June 1957 and continued for approximately 8 weeks.

Each day Navajo driver-interpreters would furnish transportation to individuals who wished to be examined and would make appointments for future examinations. In addition to the people gathered in this manner, other individuals and families appeared at the place of examination of their own volition. When the subjects presented themselves for examination a medical history was

TABLE II.—NAVAJOS EXAMINED BY AGE GROUP AND SEX

	Total examined			*Ganado*			*Pinon*		
Age group, years	*Both sexes*	*Male*	*Female*	*Both sexes*	*Male*	*Female*	*Both sexes*	*Male*	*Female*
Total	1,092	361	731	664	205	459	428	156	272
20–24	26	5	21	21	4	17	5	1	4
25–29	222	49	173	129	30	99	93	19	74
30–34	135	41	94	74	22	52	61	19	42
35–39	122	29	93	76	19	57	46	10	36
40–44	85	31	54	53	14	39	32	17	15
45–49	93	31	62	54	18	36	39	13	26
50–54	84	29	55	53	18	35	31	11	20
55–59	89	32	57	58	17	41	31	15	16
60–64	62	28	34	37	13	24	25	15	10
65–69	82	44	38	50	24	26	32	20	12
70–74	41	18	23	27	13	14	14	5	9
75 and over	50	23	27	31	12	19	19	11	8
Age unknown	1	1	0	1	1	0	0	0	0

taken. This included questions on general health with particular emphasis on questions to which the answers might reveal symptoms related to cancer. Whenever necessary, interpreters were used for this interview, and whenever practical the interview was conducted by a person of the same sex as the interviewee. After the completion of the history interview, blood was drawn for laboratory analysis. The sample was examined for hemoglobin, white count, and differential; the blood type and Rh factor were determined. Each tenth person's blood was further analyzed for the CDE—cde factor. The next step in the procedure was a general physical examination. At this time a sputum, on albumin treated slides, was obtained for Papanicolaou smear. Whenever a pelvic examination was done on the women, vaginal pool and cervical smears were made at Ganado and cervical smears were made at Pinon for the Papanicolaou examination. Finally, at Ganado, using the facilities of the Sage Memorial Hospital, a standard 14 by 17 film was taken of the chest, while at Pinon the 70 millimeter screening photoroentgen machine of the Arizona State Health Department was used.

The Papanicolaou smears were sent to the National Cancer Institute of the National Institutes of Health, Bethesda, Maryland, for interpretation. Arrangements were made for further analysis of the Cancer Institute findings by Dr. T. H. Enterline, As-

TABLE III.—PERCENTAGE OF NAVAJO POPULATION EXAMINED BY AGE GROUP AND SEX

	Male			*Female*		
Age group, years	*Population*	*No. examined*	*Per cent examined*	*Population*	*No. examined*	*Per cent examined*
Total	10,717	361	3.4	10,986	731	6.7
20–24	2,182	5	.2	2,419	21	.9
25–29	1,573	49	3.1	1,692	173	10.2
30–34	1,205	41	3.4	1,368	94	6.9
35–39	1,128	29	2.6	1,214	93	7.7
40–44	903	31	3.4	985	54	5.5
45–49	905	31	3.4	872	62	7.1
50–54	675	29	4.3	586	55	9.4
55–59	593	32	5.4	462	57	12.3
60–64	453	28	6.2	393	34	8.7
65–69	423	44	10.4	374	38	10.2
70–74	268	18	6.7	252	23	9.1
75 and over	409	23	5.6	369	27	7.3
Unknown age	0	1	0.0	0	0	0.0

sociate Professor of Surgical Pathology, University of Pennsylvania. When processing was completed, the chest films were first read by the radiologic consultant of the Arizona State Health Department and then further studied by the associates of Dr. Eugene Pendergrass of the Hospital of the University of Pennsylvania.

After the completion of the examination series the data were reviewed by the senior field officer and the personnel of the Bureau of Vital Statistics, Arizona State Health Department. Following this review the data—history, physical examinations, and laboratory findings—were coded for International Business Machines, punched, and tabulated for analysis.

FINDINGS

One thousand and ninety-two Navajos 22 years old and older were examined during the course of the project. Of these 664 were examined at Ganado, 205 males and 459 females, and 428 at Pinon, 156 males and 272 females. The method of drawing the sample from the population appears to preclude the possibility that it is statistically valid; however, it is of interest to know something about the group as related to the population from which it is drawn. The latest available information, reported by the Bureau of Indian Affairs, sets the Arizona Navajo Reservation population at 50,425. If the 50,425 Arizona Navajos follow the same age and sex pattern as the total tribal population, estimated at 81,700, and this would seem a reasonable assumption since they make up approximately 60 per cent of the group, then the segment with which we are concerned, those 20 years old and older, can be estimated on a percentage basis. Table I sets out such an estimation by age group and sex, while Table II provides similar data for those examined in this survey both in Ganado and Pinon. The percentage of the population sampled by sex and age group is shown in Table III. If the sexes are considered independently, excluding the age group 20 to 24 years, there would be only insignificant statistically valid differences in the percentage of the population sampled in the several age groups. Mean and median ages of those examined and of the estimated population, all computed on the basis of 5 year age groups, appear in Table IV. The differences, though not great, indicate that those examined were older than the general populace—thus indicating that there might be a somewhat higher incidence of cancer, more often considered a disease of older persons, in the examined group than in the total population. Until such time as a more valid sample is available the results of the survey could, with some limitations, be projected to encompass the total Navajo population.

In Table V the total is divided into the figures of the 4 examiners as to the general

TABLE IV.—MEAN AND MEDIAN AGE (YEARS) IN ESTIMATED POPULATION AND NAVAJOS EXAMINED

	Both sexes	*Male*	*Female*
Total population			
Mean age	39.8	40.6	39.1
Median age	35.9	36.8	35.6
Total examined			
Mean age	45.6	49.9	43.5
Median age	42.4	49.0	39.2
Ganado			
Mean age	45.9	49.4	44.3
Median age	43.0	48.4	40.6
Pinon			
Mean age	45.1	50.5	42.0
Median age	41.4	48.6	37.2

TABLE V.—DISTRIBUTION AS TO GENERAL APPEARANCE OF PERSONS EXAMINED

		Normal		*Thin*		*Obese*	
	Total	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
Ganado							
Male	205	166	81.0	11	5.4	28	13.6
Female	459	321	69.9	48	10.5	90	19.6
Pinon							
Male	156	153	98.1	3	1.9	0	0.0
Female	272	257	94.5	9	3.3	6	2.2

TABLE VI.—RESULTS OF PHYSICAL EXAMINATIONS AT GANADO

	Male				Female			
	Normal		Abnormal		Normal		Abnormal	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Scalp	200	97.6	5	2.4	455	99.1	4	0.9
Eye	143	69.8	62	30.2	371	80.8	88	19.2
Ear	176	85.9	29	14.1	439	95.6	20	4.4
Nose	195	95.1	10	4.9	454	98.9	5	1.1
Oral cavity	125	61.0	80	39.0	275	59.9	184	40.1
Voice	202	98.5	3	1.5	458	99.8	1	0.2
Neck	191	93.2	14	6.8	442	96.3	17	3.7
Chest	177	86.3	28	13.7	429	93.5	30	6.5
Breast	204	99.5	1	0.5	437	95.2	22	4.8
Heart	187	91.2	18	8.8	444	96.7	15	3.3
Abdomen	162	79.0	43	21.0	373	81.3	86	18.7
Lymph nodes	197	96.1	8	3.9	455	99.1	4	0.9
Extremities	170	82.9	35	17.1	409	89.1	50	10.9
Skin	197	96.1	8	3.9	438	95.4	21	4.6

appearance with special reference to the individual being thin, obese, or normal. There is striking difference between the findings at Ganado and Pinon. Inasmuch as these differences are in general characteristically found also in the physical examinations done in our present series, and in the histories, the latter being in the main taken by the Navajos working with us, one must conclude that the screening was closer in Ganado than in Pinon. However, the laboratory data and the Papanicolaou smears were of prime interest, and the validity of these can scarcely be questioned. In Tables VI and VII this breakdown is given on the screening by simple physical examination, differentiating the place of examination and the sex, in numbers and percentage of normal and abnormal findings in the various regions of the examination.

In Tables VIII and IX the findings are given by history of the pelves. It will be noted again that in the Pinon area the deviations from the normal or usual are less. Inasmuch as these histories were taken by interpreters, one must conclude that although the anomalies are few in number, they are found more frequently in the more civilized portions of the reservations. The finding at Pinon of no case of dysmenorrhea in 259 women whereas 24 of the women interviewed at Ganado admitted having pain with their periods is indeed remarkable. Universally, postcoital bleeding was denied.

In Tables X and XI are recorded the findings of the pelvic examinations, and the observations in Pinon and Ganado are compared. Here again the difference is probably in interpretation. This is especially evident in the column on the cervix. The majority of the examinations in Ganado were conducted by a qualified obstetrician-gynecolo-

TABLE VII.—RESULTS OF PHYSICAL EXAMINATIONS AT PINON

	Male				Female			
	Normal		Abnormal		Normal		Abnormal	
	No.	Per cent	No.	Per cent	No.	Per cent	No.	Per cent
Scalp	156	100	0	0.0	271	99.6	1	0.4
Eye	151	96.8	5	3.2	248	91.2	24	8.8
Ear	154	98.7	2	1.3	270	99.3	2	0.7
Nose	153	98.1	3	1.9	266	97.8	6	2.2
Oral cavity	151	96.8	5	3.2	253	93.0	19	7.0
Voice	156	100	0	0	272	100	0	0
Neck	156	100	0	0	268	98.5	4	1.5
Chest	147	94.2	9	5.8	254	93.4	18	6.6
Breast	156	100	0	0	266	97.8	6	2.2
Heart	155	99.4	1	0.6	269	98.9	3	1.1
Abdomen	151	96.8	5	3.2	263	96.7	9	3.3
Lymph nodes	155	99.4	1	0.6	272	100	0	0
Extremities	151	96.8	5	3.2	269	98.9	3	1.1
Skin	156	100	0	0.0	271	99.6	1	0.4

TABLE VIII.—PELVIC SYMPTOMS, GANADO EXAMINATIONS

	Normal		Abnormal		Not stated	
	No.	Per cent	No.	Per cent	No.	Per cent
Menstrual cycle	408	89.0	21	4.6	30	6.5
Menorrhagia	423	92.1	9	2.0	27	5.9
Metrorrhagia	410	89.3	22	4.8	27	5.9
Postcoital bleeding	432	94.1	0	0	27	5.9
Dysmenorrhea	408	88.9	24	5.2	27	5.9
Abnormal discharges	425	92.6	7	1.5	27	5.9
Pain in pelvis	401	87.4	31	6.7	27	5.9
Other pelvis disorders	331	72.1	101	22.0	27	5.9

TABLE IX.—PELVIC SYMPTOMS, PINON EXAMINATIONS

	Normal		Abnormal		Not stated	
	No.	Per cent	No.	Per cent	No.	Per cent
Menstrual cycle	249	91.5	10	3.7	13	4.8
Menorrhagia	259	95.2	0	0	13	4.8
Metrorrhagia	257	94.5	2	0.7	13	4.8
Postcoital bleeding	259	95.2	0	0	13	4.8
Dysmenorrhea	259	95.2	0	0	13	4.8
Abnormal discharges	257	94.5	2	0.7	13	4.8
Pain in pelvis	252	92.6	7	2.6	13	4.8
Other pelvis disorders	258	94.8	1	0.4	13	4.8

gist. Whereas a lacerated cervix might have been worthy of note to him, the same cervix may have been passed as normal by the physician examining in Pinon. The same is evident as concerns the uterus. By reference to Tables VI and VII, however, one notes more deviations from the normal as concerns the heart in Ganado than in Pinon, and our internist was examining in Pinon. For 1,092 individuals the blood types were determined. Of these, the majority were types O and A. No type AB individual was found, and but 5 type B. The Rh factor also deviated from that found in the general population of the United States. Only 6 Rh negative individuals were recorded in 1,092 Navajos. Approximately every tenth person was further investigated for the CDE—cde factors. Laboratory findings of blood tests are recorded in Tables XII, XIII, and XIV.

The results found in the Papanicolaou smears of the cervices are recorded in Table XV. Results of 148 cytologic examinations from Ganado indicated atypical cells in 6 cases, and probably malignant in 1 case, thus requiring further investigation of 7 individuals, or 4.7 per cent of this group. At Pinon, 6 individuals were found to have atypical cells, or 6.1 per cent of 98 examinations. Through the Arizona State Health Department and the staff of the Sage Memorial Hospital, Ganado, Arizona, 12 of these 13 individuals were located, and a conization or biopsy of the cervix was performed for each of the 12. The histopathologic diagnoses were given by T. H. Enterline. In Table XVI the diagnosis in each case is recorded. There is 1 intraepithelial carcinoma of the cervix, and 6 individuals have various combinations of basal cell hyperactivity, squamous metaplasia, and atypia.

Only 12 readable films were obtained by photoroentgen of the chest at Pinon, some 300 films resulting in no recorded image. At Ganado, all of the films were readable, and the interpretations are shown in Table XVII. Comparison of the films obtained in-

TABLE X.—PHYSICAL FINDINGS IN PELVIC EXAMINATIONS, GANADO EXAMINATIONS

	Normal			Abnormal			Not stated	
	No.	Per cent	Per cent of known	No.	Per cent	Per cent of known	No.	Per cent
Vaginal outlet	219	47.7	86.2	34	7.6	13.8	205	44.7
Vagina	224	48.8	88.5	29	6.3	11.5	206	44.9
Cervix	114	24.8	45.0	139	30.3	55.0	206	44.9
Uterus	161	25.1	66.8	80	17.4	33.2	218	47.5
Adnexa	225	49.0	93.8	15	3.3	6.2	219	47.7

TABLE XI.—PHYSICAL FINDINGS IN PELVIC EXAMINATIONS, PINON EXAMINATIONS

	Normal			Abnormal			Not stated	
	No.	Per cent	Per cent of known	No.	Per cent	Per cent of known	No.	Per cent
Vaginal outlet	124	45.6	90.5	13	4.8	9.5	135	49.6
Vagina	126	46.4	91.9	11	4.0	8.1	135	49.6
Cervix	101	37.2	73.0	36	13.2	27.0	135	49.6
Uterus	117	43.0	86.6	13	6.6	13.4	137	50.4
Adnexa	132	48.5	97.7	3	1.1	2.3	137	50.4

TABLE XII.—BLOOD TYPES OF PERSONS EXAMINED

	Ganado		Pinon	
Type	*Male*	*Female*	*Male*	*Female*
O	136	344	118	213
A	67	114	37	52
B	0	0	1	4
AB	0	0	0	0
Unknown	2	1	0	3
Total	205	459	156	272

TABLE XIII.—Rh FACTOR OF BLOODS OF PERSONS EXAMINED

	Ganado		Pinon	
	Male	*Female*	*Male*	*Female*
Positive	202	456	155	268
Negative	1	3	1	1
Unknown	2	0	0	3
Total	205	459	156	272

dicating abnormal conditions with films on file at the Sage Memorial Hospital show that the lesions regarded as being suggestive of cancer were in fact not so, in view of the recorded biologic history by previous films of the chest. Thus, no carcinoma of the lung was found in 676 chest films of Navajo Indians.

One individual was found by biopsy-resection to have basal cell carcinoma of the bridge of the nose. This woman is under treatment at the Public Health Service Indian Hospital, Albuquerque, New Mexico.

COMMENT

The finding of 1 intraepithelial carcinoma of the cervix and 6 atypical lesions of the cervix in an ethnic group of 256 individuals whose mortality rate from pelvic cancer is low gives room for speculation. Our found rate is no invasive carcinoma, 3.9 per thousand intraepithelial carcinoma, and 27.34 per thousand atypical or precancerous lesions.

Two other recent mass surveys for carcinoma are in the recent literature of the United States, and one from the German literature is cited. Nieburgs, Stergis, Stephenson, and Harbin report a mass survey of 17,761 women over the age of 19 years, residing in Floyd County, Georgia. By means of cytologic examinations, 117 of these women were found to have cells suggestive of malignancy. By biopsy, 84 of these women were found to have carcinoma of the cervix, carcinoma in situ in 56 and invasive carcinoma in 28. The morbidity for carcinoma of the cervix was thus found to be 2.8 per 1,000; and 1.4 per 1,000 had intraepithelial carcinoma. Repeat examinations over a period of 4 years indicated that new cases of carcinoma in situ developed in 1.8 per 1,000 each year. These authors believe that this rate would be valid for the population in general in the United States.

Dale, Brines, Wilson, and Nelson in a survey of women referred to a metropolitan

TABLE XIV.—Rh FACTOR BREAKDOWN OF BLOODS OF PERSONS EXAMINED

	Ganado				Pinon			
	Male		Female		Male		Female	
	No.	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
Tested	18	100	73	100	22	100	40	100
CDE	15	83.2	65	89.0	3	13.6	8	20.0
CDe	0	0	1	1.4	4	18.2	7	17.5
CdE	1	5.6	1	1.4	0	0	0	0
Cde	0	0	0	0	0	0	0	0
cDE	1	5.6	3	4.1	9	41.0	16	40.0
cDe	1	5.6	3	4.1	5	22.7	8	20.0
cdE	0	0	0	0	0	0	0	0
cde	0	0	0	0	1	4.5	1	2.5

TABLE XV.—PAPANICOLAOU SMEARS

		Normal		Probably normal		Possibly malignant		Probably malignant	
	Total	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*	*No.*	*Per cent*
Ganado									
Vaginal pool	133	111	83.4	17	12.8	5	3.8	0	0.0
Cervix	148	121	81.7	20	13.5	6	4.1	1	.7
Pinon									
Vaginal pool	2	2	100.0	0	0.0	0	0.0	0	0.0
Cervix	98	80	81.7	12	12.2	6	6.1	0	0.0

TABLE XVI.—PATHOLOGIC REPORTS ON TISSUE RECOVERED FROM 12 NAVAJO WOMEN

Tissue No.	*Pathology*
1790	Proliferative endometrium Chronic cervicitis
1791	Secretory endometrium Chronic cervicitis
1792	Endometrium not definitely phased Cavernous hemangioma of the cervix and basal cell hyperplasia with atypia, severe
1793	Secretory endometrium Chronic cervicitis with squamous metaplasia, basal cell hyperplasia and moderate atypia of the cervix
1794	Proliferative endometrium Chronic cervicitis
1795	Chronic cervicitis with squamous metaplasia
1796	Chronic cervicitis with moderate basal cell hyperplasia and severe atypia
1797	Tuberculous endometritis. Comment: This is a borderline situation. The evidence is not sufficient to diagnose intramucosal carcinoma, particularly in the presence of tuberculosis of the endometrium. Follow-up and therapy are indicated. Chronic cervicitis with squamous metaplasia, basal cell hyperplasia with marked atypia
1798	Secretory endometrium Squamous cell carcinoma (intramucosal) of the cervix
1799	Chronic cervicitis
1800	Secretory endometrium Endocervical polyp Chronic cervicitis with squamous metaplasia with focus of marked atypia
1801	Proliferative endometrium Chronic cervicitis

Cancer Detection Center, found that in 15,832 women, 151 women had carcinoma of the cervix. One hundred forty-seven of these were squamous cell carcinoma, and of these, 39 were preinvasive.

Winter, reporting in the German literature, amassed from the gynecologic clinics of 8 universities and 8 other hospitals, 4,018 cases of carcinoma of the cervix, of which 254 were intraepithelial and 3,764 were invasive. In his own clinic, he has been able to increase his finding of stage 0 carcinoma from 5 per cent to 20 per cent of carcinomas found, by the use of the Ayer type biopsy.

In our own small series, only rather broad generalizations can be made. We have a population which has been shown to have a lower rate of mortality from malignant disease. The morbidity rate of possible precancerous disease seems to be more than

TABLE XVII.—X-RAY FILMS

	Ganado		*Pinon*	
	Male	*Female*	*Male*	*Female*
Total taken	205	459	153	263
Total readable	205	459	3	9
Normal				
No.	127	333	2	7
Per cent	62.0	72.5	66.7	77.8
Tuberculosis				
No.	0	4	0	0
Per cent	0	0.9	0	0
Abnormality				
No.	72	112	0	2
Per cent	35.1	24.4	0	22.2
Suspicion of cancer				
No.	5	8	1	0
Per cent	2.4	1.8	33.3	0
Unknown				
No.	1	2	0	0
Per cent	0.5	0.4	0	0

one-fourth and approaches one-third. However, the mortality rate remains low.

The answer may lie in projecting the thesis of Erf and Miller who point out that our present knowledge of the cause, prevention, and cure of cancer is similar to the scientific knowledge of the cause, prevention, and cure of primary anemia applied to our 1925 knowledge. In 1925, the lay term for primary anemia was "cancer of the red blood cells." There are several similarities. The red cell precursors in primary anemia become bizarre in shape and size, and vacuolization is evident, as if a necessary building block is missing, and the cells are trying to make up the difference. In carcinomatosis, the cells are bizarre, with wild and misshapen nuclei, as if an element necessary for the regular orderly mitosis and the metabolism necessary for orderly division is lacking or in reduced amount.

In the Navajo, although the diet is similar to that of the population in general, it differs in some respects. As previously mentioned, the Navajo consumes the entire animal when sheep, goats, or cattle are slaughtered. It is in the realm of possibility that fresh roasted duodenum may provide a maturing element which is missing to the white population, especially missing in the cured meats which are available to us coming from duodenum and duodenal mucosa.

The lack of trauma from brassieres, the fact that infants are breast fed, and the cell maturing factor, if this be a factor, may well explain the marked infrequency of carcinoma of the breast.

The marked infrequency of carcinoma of the penis in an uncircumcized group is very striking and makes one curious as to whether the almost universal circumcision of infants as practiced in the United States today is justified.

CONCLUSIONS

1. One thousand and ninety-two men and women of the Navajo tribe of American Indians all over the age of 22 years, and all but 25 over the age of 25 years, were examined with reference to carcinoma, especially of the female pelvis and of the lung.

2. One carcinoma of the skin was found, and no carcinoma of the lung.

3. Papanicolaou smears were obtained from 256 women, with 13 of these showing cells suggestive of pelvic cancer.

4. Twelve of these women were located and appropriate biopsies performed.

5. Of these 12, one individual had tuberculosis of the endometrium, and 1 had in situ carcinoma of the cervix. Six others showed atypia, squamous metaplasia, and basal cell hyperplasia.

6. No case of carcinoma of the breast was detected.

7. The deviations from the morbidity exhibited in the general population of the United States is pointed out as between Navajo and whites and other nonwhites, in cervix, breast, endometrium, and penis.

8. It is believed by the senior authors that a factor other than genetic is responsible for the deficit of malignant disease in the Navajo, and a hypothesis for this theory is indicated.

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A STUDY OF 227 PATIENTS WITH ACUTE LARGE BOWEL OBSTRUCTION DUE TO CARCINOMA OF THE COLON

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IN MANY PATIENTS with carcinoma of the colon acute intestinal obstruction develops at some time in the evolution of the symptom complex. The obstruction may be mild and spontaneously reversible. When it persists, a serious physiologic problem is added to that of cancer. We are presenting a clinical experience of 227 patients with colon cancer complicated by large intestinal obstruction. In these cases, the disease did not permit the surgeon to follow the usual course of elective definitive resection. In every instance, there was the challenge of the urgent situation produced by acute obstruction; the patient had to be salvaged from the emergency situation before treatment of the primary disease. We were particularly interested in studying the following aspects of this problem: (1) pathologic anatomy of the obstructing lesion; (2) pathologic physiology of the acute colon obstruction; (3) presence of associated small bowel distention; (4) physiologic basis and the scope of treatment; (5) indications for emergency surgical decompression of the large bowel; (6) the use of cecostomy and transverse colostomy.

CASE MATERIAL

During the 7 year period, 1947 to 1953, there were 409 patients with carcinoma of the colon admitted to the Philadelphia General Hospital. In the 9 year period, 1945 to 1953, there were 596 patients with carcinoma of the colon admitted to Hahnemann Hospital. It was originally intended to examine these groups of patients as a homogeneous group but they were not. Philadelphia General Hospital is a large municipally owned charity hospital. Its patients generally present problems of the poor risk patient not seen in other hospitals in this city. Hahnemann Hospital is a large private metropolitan institution whose patients, though many have similar medical problems of a chronic nature, are under the care of a private physician or various outpatient clinics prior to admission.

The value in presenting these two groups will become apparent. We believe that we may categorize the Philadelphia General Hospital group as that representing the poorer risk patient rendered so because of advanced age, long standing medical complications, and generally poorer preadmission nutrition. That such categorization is accurate is evident from the statistics on operability, resectability, and over-all mortality presented in another section of this report. The group of patients from the Hahnemann Hospital we will designate as the average patient on the bases mentioned.

ANALYSIS OF DATA

One thousand and five consecutive patients with carcinoma of the colon were studied. In this group 227 patients demonstrated colon obstruction. This is said to be present when the normal passage of intestinal contents is hampered; clinically it is manifest by obstipation with varying degrees of abdominal pain and distention. Confirmatory evidence is offered by scout films of the abdomen and operative findings.

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TABLE I.—DISTRIBUTION OF NEOPLASMS WHICH CAUSED OBSTRUCTION

	No.	*Per cent of all obstructions*	*Totals, per cent*
Right segment of colon			
Cecum	9	4.1	
Ascending colon	14	6.2	
Hepatic flexure	5	2.0	
Transverse colon	18	7.8	20.1
Left segment of colon			
Splenic flexure	28	12.3	
Descending colon	26	11.6	
Sigmoid colon	66	29.1	
Rectosigmoid	41	18.1	71.1
Rectum and anus			
Rectum	20	8.8	8.8
Totals	227	100	100

Distribution of lesions which caused obstruction (*Table I*). Well over three-fourths of the obstructive lesions were in the left portion of the colon. Twenty per cent of the obstructions, however, were found to have stemmed from lesions of the right segment of the colon.

Gross lesion causing obstruction (*Table II*). The commonest gross lesion encountered was the annular constricting lesion. This was complicated in about one-fifth of the instances by necrosis and ulceration, and by variants of the inflammatory process: edema and abscess. Obturation obstruction by barium administered by mouth for diagnostic gastrointestinal series was noted in 10 patients.

What causes a chronic, slow growing constricting lesion to obstruct acutely the lumen of the bowel? Including the few obturation obstructions with those tumors demonstrating gross inflammatory changes, a credible answer is found for about one-quarter of these patients. The mechanism is a rapidly reversible one and probably accounts for the often recorded clinical observation of ease of relief of obstruction by self-administration of enemas and passage of feces and flatus following surgical decompressive operations.

TABLE II.—GROSS LESION CAUSING NEOPLASTIC OBSTRUCTION OF THE COLON

Pathology	*No. of instances*	*Per cent incidence*
Annular lesion	191	65
Necrosis, ulcer	61	21
Mucus formation	19	6
Edema and abscess	47	16
Obturation with·		
Barium	10	3.5
Fruit pits	2	1.0

Evidence of small bowel obstruction (*Table III*). About three-quarters of these patients complained of colicky abdominal pain. Somewhat less than one-half had obstipation lasting 3 to 5 days, and vomited more than once daily. Eight patients presented themselves with historical and physical features leading to a clinical diagnosis (including radiography) of apparently pure small bowel obstruction on admission. At the time of admission approximately one-fourth of these patients had distention and hyperactive peristalsis. Evaluation of the scout film of the abdomen at the time of admission demonstrated slight to marked small bowel distention in 40 per cent of these patients.

A distended small bowel, whatever the cause, must be reckoned with. Vigorous preoperative replacement with fluids and electrolytes is indicated when small bowel distention is recognized. Geriatric patients with serious metabolic, respiratory, and cardiovascular disease are affected; the complicating medical condition may be adversely affected and may decide the issue in the face of fluid and electrolyte losses caused by small bowel obstruction. Tube decompression is the mainstay of the preoperative preparation and should be included in all such cases.

Treatment (*Table IV*). In the Philadelphia General Hospital series, operative decompression was necessary in 74 per cent; 39 cecostomies and 39 colostomies were performed. The over-all mortality for each procedure was 32.5 per cent. There were 104 obstructions: 29 per cent were treated by decompressive operation only; 58 per cent by resection, including 9 primary resections for carcinoma of the right portion of the colon; 13 per cent by no surgical therapy.

In the Hahnemann Hospital series, operative decompression was necessary in 72

per cent; 65 cecostomies and 24 colostomies were done. The mortality for the colostomies was 25 per cent; for the cecostomies, 9.2 per cent.

There were 123 patients in the group who received definitive treatment: 17 per cent were treated by surgical decompression only; 79 per cent by resection; 4 per cent had no surgical therapy.

These data establish the Philadelphia General Hospital patient as a generally poor risk patient for purposes of this study: operability is lower, resectability is lower, mortality is higher with medical or surgical therapy—decompressive or resective. Colostomy or cecostomy in such a patient carried equal mortality. In the average patient, however, cecostomy offers an almost threefold better chance of survival.

DISCUSSION

These data demonstrate the changing character of the problem of obstructing colon carcinoma. While in 1945 Rankin was able to state that most of these cases of obstruction could be managed successfully with conservative nonsurgical measures, about three-fourths of the patients in this study needed surgical decompression. Rankin, as did Wangensteen (10), alluded to the appearance of small bowel distention as a late sign in the syndrome of large bowel obstruction. It was recognized that small intestinal obstruction could result from direct extension of the malignant and inflammatory process of the colon. No emphasis was placed, however, on the more subtle types of small bowel distention due to either malfunction or dysfunction of the ileocecal colic segment.

The general belief has been that the ileocecal valve prevents regurgitation of colonic material and gas into the ileum and so accounts for the "closed loop" obstruction in the colon. Allegedly, 10 per cent of these ileocecal valves are incompetent because the inferior leaflet is absent. In such cases the obstructed colon supposedly decompresses itself into the small intestine. In our experience, a much larger percentage of acute colon obstructions (about 40 per cent) exhibits signs of associated small bowel obstruction, and scout films of the abdomen often show loops of small bowel with gas and fluid levels. Actually, in 20 per cent of our cases of obstruction there was moderate to marked gas distention of the small bowel. At operation for emergency decompression of the obstructed colon, the presence of small bowel distention verifies the clinical and roentgen findings.

TABLE III.—SIGNS AND SYMPTOMS SUGGESTIVE OF SMALL BOWEL OBSTRUCTION IN 227 PATIENTS WITH NEOPLASTIC COLON OBSTRUCTION

	No.	*Per cent*
Colicky abdominal pain	209	72
Vomiting more than once daily prior to admission	144	49
No bowel movements 3 to 14 days	120	42
Hyperactive peristalsis	61	26
Feculent vomiting	17	6

If this distention is due to an incompetent ileocecal valve why are the cecum and colon tightly distended and very little decompressed at the time of decompressive surgery? Our anatomic and physiologic studies would indicate that the ileocecal orifice is not only a valve but a functional papilla (4, 9). Anatomically, absence of a valve leaflet is uncommon. Actually, in normal and even in pathologic circumstances the ileocecal orifice is probably uncommonly incompetent.

We have evidence that the material in the obstructed colon of the experimental animal does not come from large bowel putrefaction and secretion. Experimentally, the total colon closed at both ends with ileal emptying diverted into the rectum will survive indefinitely without critical distention or circulatory embarrassment (6, 8). The gas, which is largely nitrogen, and the fluid which accumulates come largely from ileal emptying into the colon. It is doubtful that the obstructed colon generates gas and fluid to a pressure large enough to interfere with the circulation of the bowel wall or to force open the ileocecal valve. Just as Wangensteen (11) demonstrated in the small bowel,

the majority of the material in the large bowel is of extrinsic origin; changes in the large bowel develop as a result of the dysfunction in the terminal ileum. It is this segment of bowel in the patient with the diseased colon that offers resistance to the gradient of emptying from the small bowel into the large bowel. At the same time, it is this segment that continues to empty into the obstructed colon. The result is not only a closed loop obstruction but what we would term a "tension closed loop obstruction" arising from the greater sensitivity and the greater muscular activity and contractility of the terminal ileum and the ileocecal papilla in comparison with the right segment of the colon or cecum. Except in cases of barium enema, the pressures in the right segment of the colon never approach the larger pressures that exist in the terminal small intestine.

These pathophysiologic considerations should be reflected in our therapeutic approach to the problem, as indicated previously (7). First of all, probably in every case a certain degree of small bowel obstruction exists. Consequently, Levin tube and long tube suction are of tremendous immediate importance in the emergency treatment and preparation of the patient. This decompression helps prevent the continued emptying of the terminal ileum into an already distended colon. Regardless of the improvement achieved with the suction for the small bowel, it is important to keep in mind the concept of tension closed loop in the colon. If there is not relief of the obstruction in the large bowel in a matter of 12 to 24 hours, then surgical intervention becomes imperative.

It is difficult to see how there can be a controversy between the conservative regimen of therapy and surgical decompression. Our experience would indicate that one cannot do without the other. The conservative regimen should be instituted as an emergency in these seriously ill patients. Time must be taken for supportive therapy, tube suction, and antibiotic and antispasmodic medication. Of equal importance is the time necessary to make a complete diagnosis not only of the intestinal situation but also of the entire medical status of the patient, particularly the cardiovascular, metabolic, nutritional, and hematologic status. Usually in 12 to 24 hours the patient is vastly improved. The medical and surgical diagnosis is clarified. In 25 per cent of the cases the conservative regimen may obviate the necessity for surgical decompression preliminary to resection. In approximately three-fourths of the patients, surgical decompression is indicated because no flatus has been passed and there is no indication that the obstruction in the large bowel has relented to any degree. In patients who are well prepared surgical decompression will be more successful with less morbidity and mortality. Furthermore, in a certain number of patients it may be possible to do a definitive resection, particularly with lesions of the right segment of the colon and the cecum.

Most interesting to consider is the place of surgical decompressive measures, specifically cecostomy and transverse colostomy. The Philadelphia General Hospital series demonstrates no apparent advantages in choice of one operation over the other to treat an obstructed colon in a poor risk and depleted patient. In the average situation, however, cecostomy is safer and as effective a decompressive maneuver. Our clinical and experimental studies support this contention (5). Further, there is evidence to support the statement that cecostomy for decompression followed by resection is an effective and safe course of therapy (Table IV). Mortality is considerably lower when this plan is followed in *both* the poor risk and the average patient.

It has been taught that obstruction complicating carcinoma of the colon carries a graver prognosis than uncomplicated colon carcinoma. Colcock in a recent publication presented the current surgical statistics for uncomplicated carcinoma of the colon: operability nearly 100 per cent, resectability

TABLE IV.—SURGICAL TREATMENT AND MORTALITY IN 227 PATIENTS WITH COLON OBSTRUCTION DUE TO CARCINOMA

	Philadelphia General Hospital series					*Hahnemann series*				
Treatment	*Patients*	*Operations*	*Deaths All*	*Deaths Operative*	*Per cent mortality*	*Patients*	*Operations*	*Deaths All*	*Deaths Operative*	*Per cent mortality*
Surgical decompression alone										
Colostomy	17		7			9		4		
Cecostomy	14		10			7		3		
Total	31	31	17	17	55	16	16	7	7	43
Resection										
Decompression followed by resection:										
Colostomy and resection	22		5		43	15		2		13
Cecostomy and resection	25		2		12.5	58		3		5.1
Total	47	94	7		14.8	73	146	5		6.8
Primary resection (right colon) following tube suction decompression	14	14	1		7.1	24	24	1		4.1
Total all resections	61		8	8	7.6	97		6	6	6.1
Other operations	6*	13	2	2		6†	11	1	1	
No surgical therapy	6		5			5		4		
Over-all totals	104		32		30.8	124		18		14.5
All operative totals		152		27	17.7		197		14	7.1

*Colostomy followed by colocolostomy—2; cecostomy followed by colostomy—3; cecostomy followed by colostomy followed by resection—1.
†Ileotransverse colostomy in continuity followed by resection—1; cecostomy followed by colostomy—4; cecostomy followed by colocolostomy—1.

over 90 per cent, and mortality for resection about 5 per cent. Our data demonstrate that these goals may be approached today in the average patient with obstruction. Even in the generally poor risk patient operative mortality for resection approaches this level. These facts document the necessity and effectiveness of modern surgical decompression and staged resection together with adequate preoperative preparation.

We have no data for primary resection of obstructing carcinoma of the left segment of the colon; there were none in this series. The effectiveness of long tube therapy preliminary to primary resection of the right segment of the colon in obstruction is, however, again demonstrated as by Ravdin and Abbott. This operation was performed with minimal mortality to the patients in this particular series.

Standardization of the therapy for obstructing carcinoma of the colon is another recent development. Obstruction resection has given way to staged surgical decompressive operations followed by resection with end-to-end anastomosis of the colon. Side-tracking in-continuity procedures were rare in this series (4 in 349 operations). There were, however, an appreciable number of "palliative" colostomies. That these are *not* palliative is apparent considering the average mortality of 42 per cent when this operation is elected. We believe that the surgeon should make every effort to achieve resection for palliation in this type of patient.

SUMMARY

1. Two hundred and twenty seven patients with obstructing colon carcinoma are presented as two approximately numerically equal groups from different institutions.

2. These institutional groups are categorized as poor risk and average on the basis of operability, resectability, and mortality differences.

3. Observations of the surgical behavior of the poor risk and average patient with this disease are discussed.

4. Distribution of lesions, the state of the gross lesion, evidence of complicating small bowel distention, and treatment are described and discussed.

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THE MULTICENTRIC ORIGIN OF CARCINOMAS OF THE FEMALE ANOGENITAL TRACT

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THE BELIEF that malignant tumors originate unicentrically at a single point in time, from a single cell or small group of cells, and enlarge only by intrinsic growth is under attack. There is increasing evidence from long term clinical and histologic follow-up in different groups of patients that malignant tumors arise from multiple independent foci, within an organ, paired organs, or organ system, from altered or potentially altered neoplastic "fields," and that growth is accomplished both by cellular proliferation and by progressive neoplastic conversion of cells within the altered fields. This concept is not new. It has been championed most prominently by Cheatle (6), Cheatle and Cutler (7), Muir, and Nicholson for tumors of the breast, Brunschwig (4, 5) and Willis (24–26) for tumors of the skin, Slaughter for tumors of the head and neck area (20, 21), and Gall and his associates for tumors of the stomach, lung, and breast (8, 15, 19).

The likelihood that a similar biologic phenomenon exists in the anogenital area, vagina, and cervix was suggested when a patient (Case 4) who had multiple, histologically similar, lesions of the fourchette, vulva, vagina, anal tags, and cervix, evolving over a period of years, was seen at The George Washington University Hospital. A search for previously reported cases of combined lesions of vulva and cervix revealed scattered reports, viz., those of Brown and associates and Watson, and some others involving the cervix and the vagina, including the one of May, rather than the cervix and the vulva.

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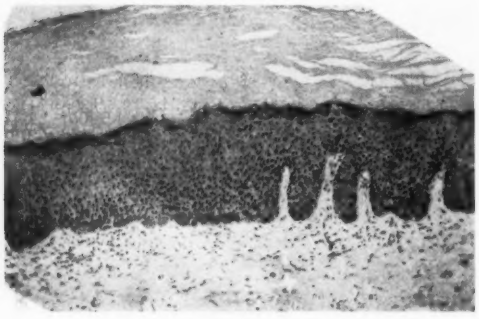
METHOD OF STUDY

This study is based upon the histologic examination of biopsy, surgical, and autopsy material from 6 patients. They were gathered by examining the pathologic reports and reviewing the slides of all patients with diagnoses of Bowen's disease, erythroplasia of Queyrat, malignant dyskeratosis, or leucoplakia of the vulva, vagina, or anal tags. In some instances cervical biopsies had been done and these slides were reviewed. The clinical record of each patient was then searched until her present status was known. The referring physician was then contacted and asked to obtain additional biopsy material from the cervix. This has now been done in an additional 10 patients, and these plus the 4 surviving patients reported in this article constitute the nucleus of a group to be reported on at a later date.

DEFINITION OF TERMS

For the purposes of this article, the "sexual skin" consisting of vulva and perianal area has been separated from the remainder of the integument and together with the vagina and exocervix defined as an "organ system." The studies of Meyer on the embryologic derivation of the vagina and exocervix from the urogenital sinus are the underlying basis for this method of grouping.

The term in situ epidermoid carcinoma is used when the histologic section shows anaplasia without invasion in the form of increased numbers of mitotic figures and loss



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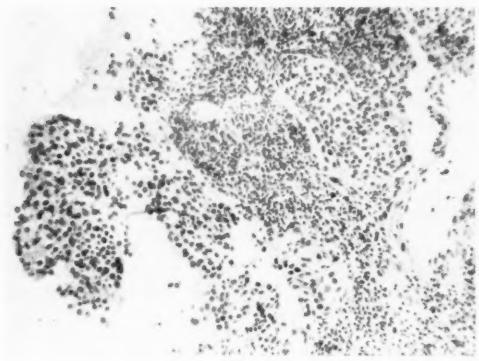


b

FIG. 1. All slides were stained with hematoxylin and eosin. Case 1. a, In situ epidermoid carcinoma of vulva. Marked acanthosis (April 1949). ×45. b, Invasive epidermoid carcinoma of cervix. (March 1954). ×155.

of polarity throughout the entire thickness of the epithelial or mucosal surface in preference to eponymic or descriptive diagnoses. Thus our use of the term in situ epidermoid carcinoma includes Bowen's disease, erythroplasia of Queyrat, malignant or premalignant dyskeratosis, precancerous dermatosis, preinvasive carcinoma, and malignant leucoplakia. Where the basement membrane has been breached, the designation invasive epidermoid carcinoma is used.

Leucoplakia includes acanthosis, parakeratosis, and a dense inflammatory exudate, primarily lymphocytes and mononuclear macrophages, closely applied to the basement membrane, together with basal layer dyskeratosis and loss of polarity. It differs from in situ carcinoma in that the anaplasia does not extend through the entire thickness of the epithelium or mucosa but is limited to the basal layers. It is regarded as an antecedent of in situ carcinoma which in turn is always present as a prelude to invasion.

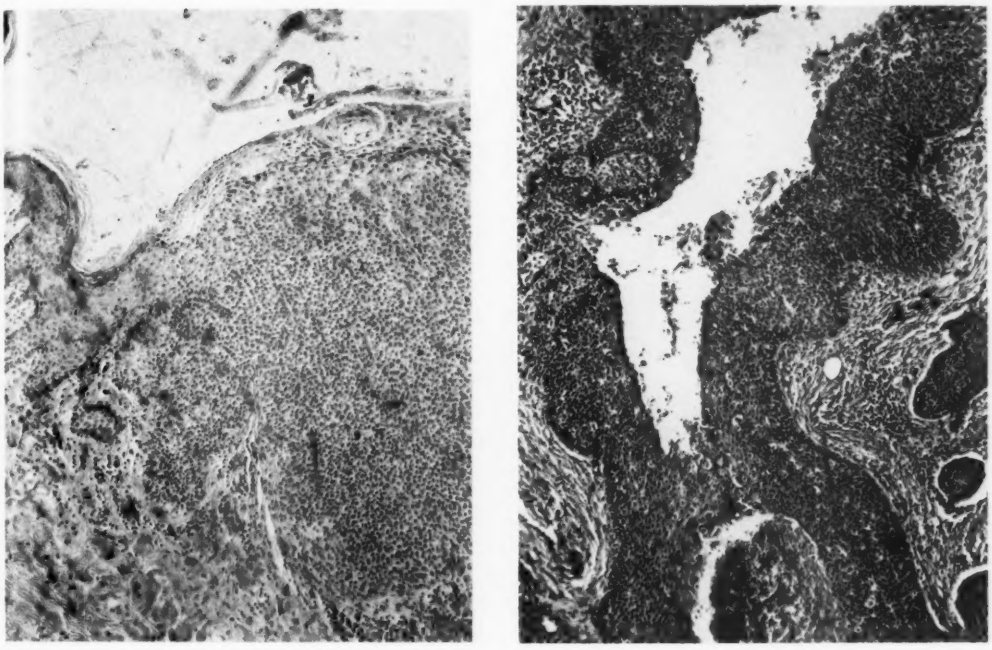
CASE HISTORIES

Chronologic résumés of the case histories of 6 patients with diagnoses of combined epidermoid carcinoma either in situ or invasive of the genitoanal area and cervix are described.

CASE 1. A white female, 80 years old, received 4 radium treatments for leucoplakia of the vulva during 1948. On April 6, 1949, a vulvectomy was performed. The slides prepared from the surgical specimen were diagnosed as in situ epidermoid carcinoma of the vulva (Fig. 1a) and perineal skin. On March 27, 1954, a biopsy of the cervix was performed because of bleeding. The diagnosis was invasive epidermoid carcinoma (Fig. 1b). Radiation therapy failed to control her disease and the patient died on October 3, 1954, with widespread metastasis. Autopsy diagnosis was epidermoid carcinoma of the cervix with metastases to uterus, tube, omentum, and pelvic lymph nodes.

CASE 2. A white female, 71 years old, was first seen on March 22, 1950, with an ulceration of the vulva of 1 year's duration. On examination, a large lesion on the right side of the introitus involving vaginal mucosa was seen. A biopsy from a margin of the vulvar lesion was diagnosed as invasive epidermoid carcinoma. A cervical biopsy performed at that time was negative. On June 16, 1950, vulvectomy was performed. The surgical specimen was diagnosed as invasive epidermoid carcinoma of the vulva (Fig. 2a). Another vulvar lesion was excised on August 24, 1950, and 43 days later a second "recurrence" was excised and a bilateral groin dissection performed. The diagnosis was epidermoid carcinoma of the vulva with metastasis in regional lymph nodes. A third "recurrence" was excised 8 months later. On October 9, 1951, an anterior evisceration was performed following a biopsy. This specimen showed in situ epidermoid carcinoma of the vagina and invasive epidermoid carcinoma of the cervix (Fig. 2b). The patient died with uremia 8 months later with widespread metastatic disease involving colon, kidney, liver, lungs, pleura, and pericardium, and the local growth about parametria, ureters, and lymph node distribution indicated that the cervical carcinoma rather than the vulvar lesion was the chief offender.

CASE 3. A white female, 27 years old, was seen in 1951 with a lesion of the vulva of 5 years' duration. One month later, when it became painful



a b

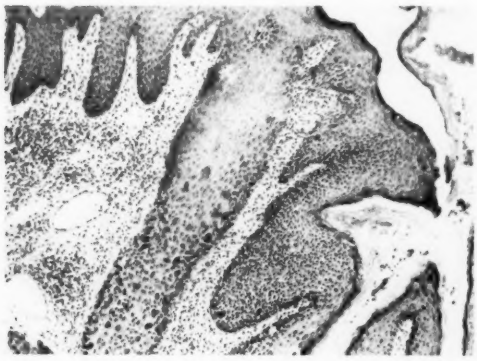
FIG. 2. Case 2. a, Margin of invasive epidermoid carcinoma of vulva (June 1950). ×50. b, Invasive epidermoid carcinoma of cervix (October 1951). ×200.

irritated, and edematous, a radical vulvectomy was performed on October 9, 1951. This specimen was diagnosed as invasive epidermoid carcinoma of the vulva (Fig. 3a), leucoplakia of the vagina, and areas of atypism in Bartholin gland ducts (Fig. 3b). A biopsy of the cervix on April 10, 1952, was diagnosed as in situ epidermoid carcinoma. Total hysterectomy was performed on April 30. Residual areas of in situ epidermoid carcinoma of the cervix were present in the surgical specimen (Fig. 3c). When the patient was last seen, she had no evidence of disease.

CASE 4. A white female, 34 years old, had in situ epidermoid carcinoma of the fourchette diagnosed by biopsy on August 7, 1951 (Fig. 4a). On March 11, 1954, a diagnostic curettage, cervical biopsy, bartholinectomy, and partial vulvectomy were performed. The surgical specimens were diagnosed as in situ epidermoid carcinoma of the vulva (Fig. 4b) and in situ epidermoid carcinoma of the cervix. On May 27, 1954, additional Schiller positive sites in the vulva and vagina were excised and total hysterectomy was performed. The microscopic diagnosis was in situ epidermoid carcinoma of the cervix with extension into endocervical glands (Fig. 4c), endometriosis, Bowen's disease in all specimens from the vulva and vagina except the fourchette. The last operation on March 8, 1956 included a resection of an area of the vagina (Fig. 4d), hemorrhoidectomy (Fig. 4e), and fissurectomy. The patient is alive and well.

CASE 5. A white female, 46 years old, had a total hysterectomy and a bilateral salpingo-oophorectomy for in situ epidermoid carcinoma of the cervix on January 2, 1957. The surgical specimens contained residual areas of in situ epidermoid carcinoma of the cervix with glandular extension (Fig. 5a), chronic cervicitis, and leiomyoma and endometriosis of the uterus. At prior cervical biopsy on December 4, 1956, a diagnosis of in situ epidermoid carcinoma of the cervix (Fig. 5b) had been made. She had had a vulvectomy for carcinoma of the vulva in 1952 during a pregnancy. The vulvectomy specimen contained in situ epidermoid carcinoma of the vulva (Fig. 5c). The patient is alive and well at the present time with no evidence of disease.

CASE 6. A white female, 33 years old, had a partial vulvectomy, partial vaginectomy, and total hysterectomy on June 10, 1956 for extensive lesions of the vulva, vagina, and cervix. The surgical specimens showed in situ epidermoid carcinoma of the vulva (Fig. 6a), leucoplakia of the vagina, and in situ epidermoid carcinoma of the cervix (Fig. 6b). Surgery had been advised initially but refused. Pelvic examination 2 months after the initial examination indicated extension of the superficial vulvar lesion to include



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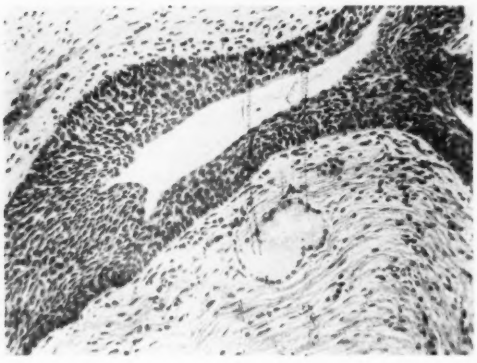

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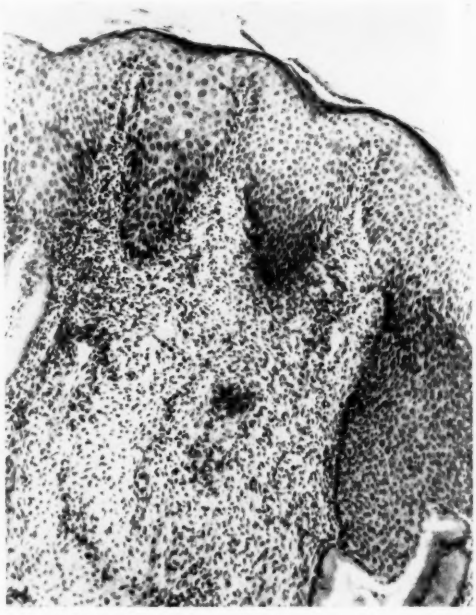

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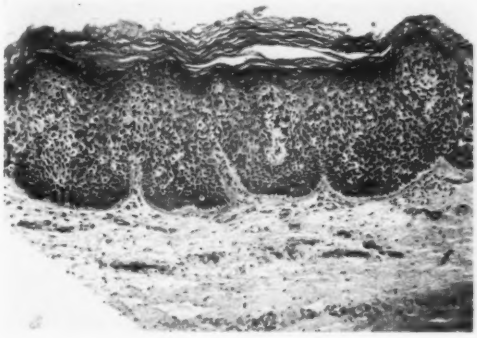
FIG. 3. Case 3. a, Margin of epidermoid carcinoma of vulva (October 1951). There was invasion in this specimen, not shown. ×77. b, Marked atypism in Bartholin gland duct. Removed at same procedure as in "a." ×155. c, In situ epidermoid carcinoma of cervix with glandular extension (April 1952). ×100.

the perineal skin and right side of the introitus and vaginal wall. There was also involvement of the cervix and vaginal vault. Following this examination the patient accepted surgery. Convalescence was uneventful, and the patient has remained well.

RESULTS AND METHOD OF TREATMENT

The youngest patient in this group was 27 years of age; the oldest, 80. Three patients in this group (Cases 2, 3, and 5) were treated initially for invasive epidermoid carcinoma of the vulva and 3 cases (Cases 1, 4, and 6) for in situ epidermoid carcinoma and leucoplakia of the vulva. The first microscopic evidence of cervical carcinoma in these 6 patients was obtained 60 months, 15 months, 7 months, 31 months, 50 months, and 18 months respectively from the date of the diagnosis of the vulvar disease. The vulvar lesions in the 6 patients in this group were treated by simple vulvectomy in 4 cases (Cases 1, 2, 5, and 6), by radical vulvectomy in 1 case (Case 3), and by partial vulvectomy in 1 case (Case 4). One of the patients (Case 2) treated by simple vulvectomy subsequently had 3 local excisions and a groin dissection for additional areas of disease. The patient (Case 4) treated by partial vulvectomy had 2 local excisions for new disease. The cervical carcinomas were treated by irradiation in 1 case (Case 1), by total hysterectomy in 3 cases (Cases 3, 4, and 6), and by total hysterectomy plus bilateral salpingo-oophorectomy in 1 case (Case 5). One patient (Case 2) was ultimately treated by anterior evisceration after vulvectomy, 3 local excisions and a groin dissection failed to control her vulvar disease. The surgical specimen contained a separate carcinoma of the uterine cervix, and she died as a result of metastasis from the cervical primary rather than the vulvar lesion.

FIG. 4. Case 4. a, In situ epidermoid carcinoma of fourchette. (August 1951). ×60. b, In situ epidermoid carcinoma of vulva (March 1954). ×100. c, In situ epidermoid carcinoma of cervix with glandular extension (May 1954). ×100. d, Schiller positive area in vagina showing leucoplakia (March 1956). ×54. e, In situ epidermoid carcinoma, hemorrhoid. (March 1956). ×77.



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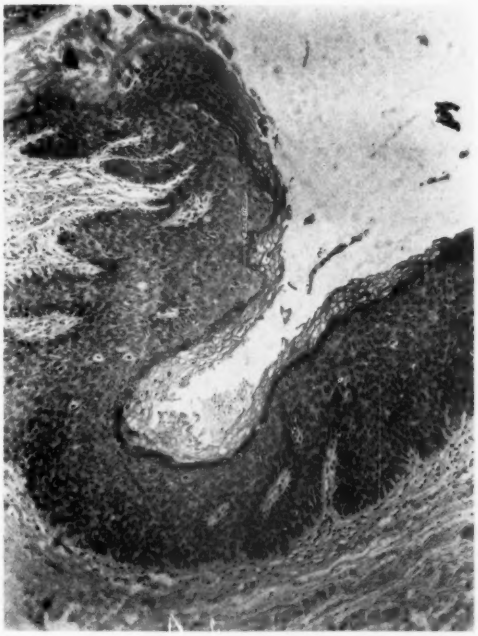

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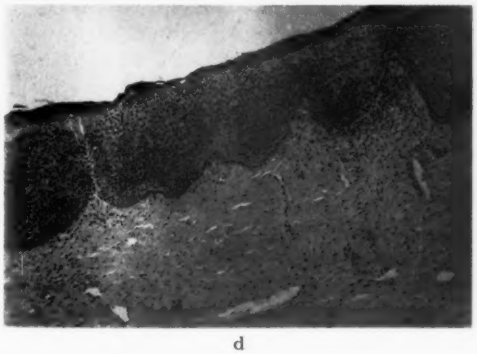

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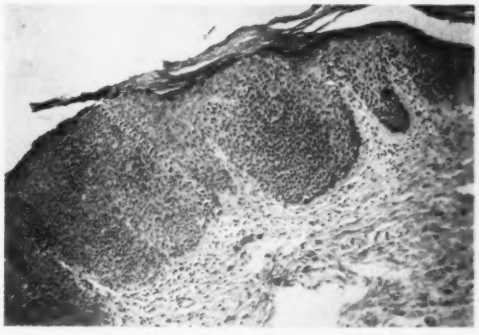

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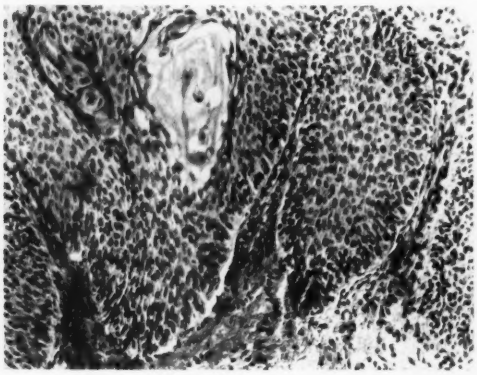

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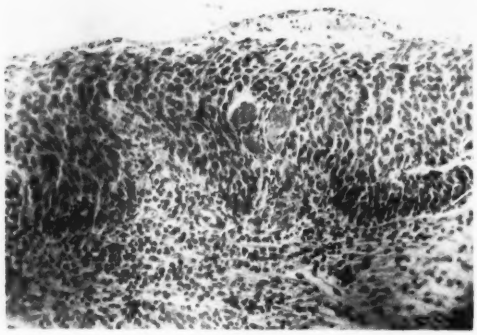


b

c

FIG. 5. Case 5. a, In situ epidermoid carcinoma of cervix with glandular extension (January 1957). ×126. b, In situ epidermoid carcinoma of cervix in biopsy specimen (December 1956). ×88. c, In situ epidermoid carcinoma of vulva (October 1952). ×60.

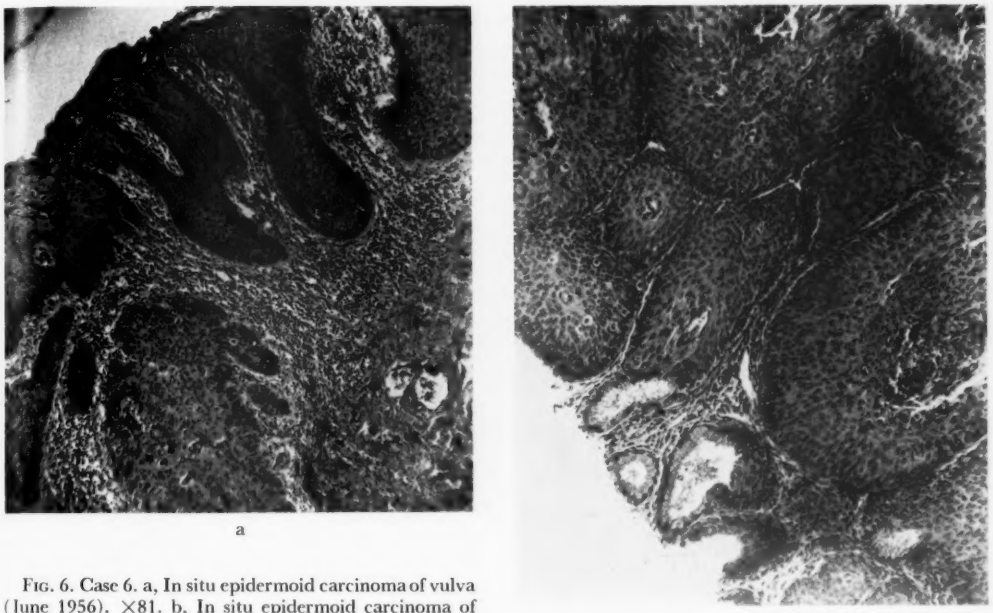
Figures 7 and 8 are intended to represent the type of case we are following as a continuing project. In December 1950, this patient was found to have invasive epidermoid carcinoma of the cervix (Fig. 7). In January 1952, a lesion of the vulva (Fig. 8) developed. This latter area does not show anaplasia through the entire thickness of the epithelium, but the beginning areas of atypism and loss of polarity in the basal layers suggest that she be followed up closely.

A group of 10 patients with in situ carcinoma of the anogenital area, plus the 4 living patients[1] described in the present article, constitute the nucleus of a series to be followed on a long term basis. One of the 10 patients in the follow-up group (age 48) has presented herself with a second area of Bowen's disease in another part of the vulva. There has been a 4 year interval between these two lesions. Biopsy of the cervix shows basal layer hyperplasia at the present time.

[1]In 1955, Dr. C. Bernard Brack of the Johns Hopkins Hospital was apprised of our findings. In a recent letter he informs us that as a result of a search for patients of the type we are reporting here, there have been 4 such cases found at the Johns Hopkins Hospital. Three of these were patients with invasive epidermoid carcinoma of the cervix in whom in situ epidermoid carcinoma of the vulva developed 1 to 4 years later. In the fourth patient invasive epidermoid carcinoma of the cervix developed 4 years after treatment for in situ epidermoid carcinoma of the vulva.

DISCUSSION

There are direct clinical applications to be made from this group of cases and from the concept of the multicentric or "field" origin of cancer as applied to an organ, paired organs, or "organ systems." The findings in these women suggest that patients with lesions of the anogenital area (vulva, vagina, and perianal skin) whether



a b

FIG. 6. Case 6. a, In situ epidermoid carcinoma of vulva (June 1956). ×81. b, In situ epidermoid carcinoma of cervix with glandular extension (June 1956). ×90.

reported as Bowen's disease, erythroplasia of Queyrat, malignant leucoplakia, precancerous dermatosis, preinvasive carcinoma, carcinoma-in-situ, or invasive epidermoid carcinoma should routinely have a biopsy of the cervix; and further, that patients who have had either in situ epidermoid carcinoma or invasive epidermoid carcinoma of the cervix should be followed closely for signs of new primary tumors of the vulva, vagina, and perianal skin areas. The "field" origin theory underscores the need for a critical evaluation of some present day concepts of the growth and spread of malignant human disease such as "recurrent" carcinoma and the improbable theory of "drop" or "mucosal" metastasis. Although these cases deal with the anogenital area, vagina, and cervix, we believe they are merely the expression at this site of a general biologic phenomenon in the growth of malignant disease in man. Inherent in the thesis of the multicentric origin of cancer are the concepts that all invasive cancer has an antecedent in situ phase prior to invasion, as expressed by Stewart, and further that a competent observer is able to tell from the presence or absence of in situ change in epithelium or mucosa whether a tumor is primary or metastatic at a given site. This latter salient feature appears to have been neglected in the ready acceptance of the notion of "recurrent" or metastatic carcinoma rather than interpreting "recurrence" as persistent or new disease in previously sensitized fields. It seems likely that some articles which feature the word "recurrence" in their titles are manifestations of this phenomenon of "field cancerization," for example, the articles by Blumberg and Ober and Graham and Meigs (11, 12).

One cannot decide without an adequate biopsy which includes overlying epithelium or mucosa whether "recurrence" represents residual areas of carcinoma not removed during the initial procedure or whether they are not in fact new areas of carcinoma developing in previously sensitized fields. Adequate numbers of sections must be taken

FIG. 7. Invasive epidermoid carcinoma of cervix (December 1950). ×30.

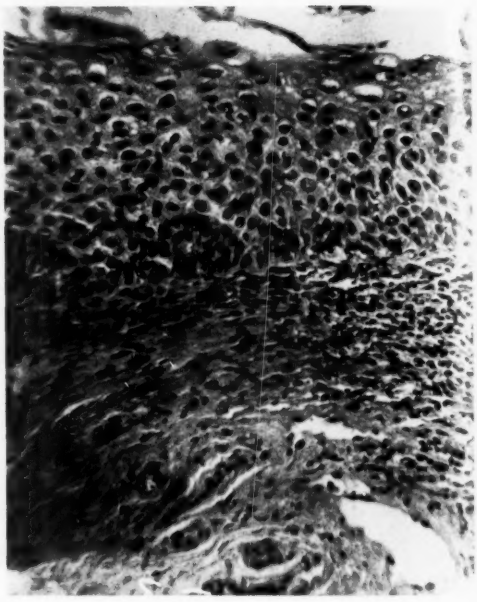


FIG. 8. Leucoplakia of vulva was present (January 1952). ×170.

from the margins of the initial surgical specimen to determine whether in situ carcinoma or areas of marked atypism were present in the original tissues removed. The second biopsy must then include a mucosal or epithelial surface, for this is the only way in which a decision of a new primary tumor versus metastatic disease can be arrived at. This point has been emphasized by Allen and Spitz in evaluating primary versus metastic melanocarcinoma and by Farrow for carcinoma of the breast.

The value of finding antecedent in situ carcinoma appears to have been minimized, neglected, or overlooked once invasion has taken place. One would suspect from reading many articles that the phenomenon of invasion obscures, destroys, or invalidates the available, easily noted evidence of antecedent, ever-present, in situ carcinoma in the specimen. More attention needs to be focused on the spectrum of in situ carcinoma or atypical epithelia or mucosae that are present at the margins or periphery (and indeed within areas showing invasion) of resected specimens. Such detail would probably decrease the number of unanticipated events in "successfully" treated cancer patients that are reported.

We have emphasized histologically similar malignant lesions occurring in an organ, paired organs, or "organ system," believing that this potential has been shown to be far higher and of greater clinical significance than the attempts to prove a supposed increased probability of histologically dissimilar primaries in different organs or organ systems.

Accordingly, we have not quoted from the extensive literature that is accumulating which deals with histologically dissimilar primaries occurring in different organs or organ systems. An excellent review of this literature can be found in a recent paper by Epstein and Shaw, and in earlier papers by Slaughter (20, 21).

We would emphasize, as have others, that the multicentric "field" origin theory is not to be misconstrued as a plea for extending the scope of surgery or increasing the num-

ber of "prophylactic procedures," but rather as a stimulus to more frequent, systematic, periodic, postoperative examination of patients, with particular attention to that organ, paired organ, or "organ system" in which the first primary carcinoma has developed.

SUMMARY

1. The case histories of 6 patients with combined, histologically similar malignant lesions (epidermoid carcinoma) of the anogenital areas and cervix are presented.

2. These cases suggest that a patient with malignant lesions of the vulva, vagina, or perianal tags should routinely have biopsies of the cervix.

3. Patients with in situ epidermoid carcinoma or invasive epidermoid carcinoma of the cervix should be examined at frequent intervals with particular attention focused on the vagina, vulva, and perianal areas with early recourse to biopsy.

4. The concept of "recurrence" versus new disease is discussed briefly.

5. Some implications of the multicentric "field" origin theory of cancer are discussed.

6. These cases are considered the expression at particular sites of a general underlying biologic phenomenon in the growth and progression of malignant disease in man.

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POLYPOID GASTRIC HETEROTOPIA OF THE JEJUNUM AND ILEUM CAUSING SUBACUTE INTESTINAL OBSTRUCTION

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THE OCCURRENCE of heterotopic gastric mucosa in the small intestine, exclusive of congenital diverticula, is distinctly rare. A report of 4 cases of symptomatic polypoid gastric heterotopia in which the surgical findings suggested true adenomatous polyps of the small intestine is presented herein.

GENERAL BACKGROUND AND REVIEW OF LITERATURE

The exact incidence of different types of heterotopic tissue in the small intestine is not known but presumably, as is true of benign tumors of the small intestine, it is considerably greater than is indicated by the figures derived from surgically removed tissues. River and associates, in a collective review of 1,399 benign neoplasms of the small intestine, stated that such tumors were found 15 times more often in a group of 1,000 necropsies than in a like number of surgical specimens. Barbosa and coworkers gave an incidence of 1.7 per cent for pancreatic heterotopia found at routine necropsies during a 5 year period at the Mayo Clinic.

The finding of ectopic gastric mucosa in the esophagus, Meckel's diverticulum, diverticula of the jejunum and ileum, and duplication of the small and large intestine is not unusual. Although we have encountered 4 examples of clinically significant polypoid gastric heterotopia of the small intestine in a 4 year period, a review of the literature revealed only 6 previously recorded examples of this condition in the jejunum and ileum (exclusive of various types of diverticula and duplication).

The first report of polypoid gastric heterotopia of the small intestine in the United States was made in 1938 by Kimpton and Crane. These authors described a 6 year old white girl who, since the age of 3 years, had experienced episodes of intermittent obstruction of the small intestine. At operation, a polypoid mass 3 centimeters in diameter was found on the mesenteric aspect of the jejunum, 20 centimeters from the ligament of Treitz. This mass had resulted in intussusception. The lesion consisted of redundant folds of mucous membrane composed of gastric glands containing chief and parietal cells.

In their discussion, Kimpton and Crane referred to 3 cases previously reported in the European literature. The first of these was presented by Poindecker, in 1912, as an instance of gastric heterotopia in the ileum of a 9 year old girl who had evidence of obstruction of the small intestine. Histologic examination of the lesion revealed gastric glands containing chief and parietal cells. The second example occurred in a 17 month old boy described by Taylor in a paper written in 1927 concerning epithelial heterotopia of the alimentary tract. This child died after multiple episodes of intestinal hemorrhage. Necropsy disclosed a tumor on the mesenteric border of the ileum 10 centimeters above the ileocecal valve. The mass consisted of redundant gastric

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mucosa containing chief and parietal cells. Adjacent to the tumor in the ileal mucosa was an ulcer 1 centimeter in diameter. The third example, reported by Barták, in 1932, was an asymptomatic nodule in the jejunum discovered during an operation for gastric ulcer. This nodule was said to involve all layers of the intestinal wall and to be composed of gastric glands and elements that resembled pancreatic acini. The gastric glands were found to contain chief and parietal cells. The appearance of the overlying intestinal mucosa in this specimen was not described.

In 1953, Gore and Williams presented the findings in a 16 year old white girl who gave a 13 month history of intermittent low grade obstruction of the small intestine associated with one episode of melena. Surgical exploration disclosed an intraluminal intussuscepting mass located in the jejunum 15 centimeters below the ligament of Treitz. The surgical specimen contained a mucosal mass extending along the long axis of the antimesenteric aspect of the intestine that measured 12 by 7 by 2 centimeters. The redundant folds consisted of gastric mucosa admixed with islands of jejunal mucosa. Chief cells were found but parietal cells were absent. The authors described pronounced polypoid hyperplasia and considered the aberrant tissue to have arisen by a process of metaplasia in an adenomatous polyp.

The sixth case was reported by Ramsay, in 1954, and concerned a 9 year old white girl who had experienced episodes of colicky abdominal pain for 2 months. Surgical intervention disclosed subacute obstruction in the lower portion of the jejunum secondary to a polypoid mass on the mesenteric border. The tumor was confined to the mucosa, measured 3.8 by 5 centimeters and was described as rugose in appearance, resembling gastric mucosa. Microscopically, the mucosa was found to be thickened and was composed of gastric glands which were lined by chief, parietal, and goblet cells.

REPORT OF CASES

CASE 1. A 28 year old white male came to the Mayo Clinic in November 1952 because of intermittent abdominal pain associated with nausea and vomiting for 4 years. He had been in good health until October 1948, when he first experienced pain in the left lower quadrant of the abdomen that often awakened him early in the morning and occurred every 4 to 6 weeks. These attacks lasted 3 to 4 days and often were associated with vomiting about 30 minutes after eating. The pain was described as sharp and constant. Roentgenograms of the gastrointestinal tract were said to be normal at that time. Approximately 6 weeks after the onset of the abdominal pain, appendectomy had been performed without relief of symptoms. Four months before admission to the clinic, the attacks of pain had become more frequent and severe. At no time did the patient have hematemesis or melena.

Contrast roentgenograms of the small intestine made at the clinic revealed intussusception just distal to the ligament of Treitz that was associated with obstruction and that suggested the presence of a tumor.

Operation disclosed intussusception in the upper part of the jejunum 12 centimeters below the ligament of Treitz. After reduction of the intussusception, palpation revealed a boggy mass in the intestinal lumen. A 10 centimeter segment of jejunum was resected, and end-to-end jejunojejunostomy was done. The operative specimen revealed 2 rugose mucosal masses on the antimesenteric aspect of the intestine. The larger one measured 2 by 1 by 5 centimeters and consisted of a serpiginous circular ridge of freely movable mucosal tissue encircling a zone of normal-appearing mucosa measuring 4 by 3 centimeters. The smaller mass was somewhat villoid in appearance, sessile, and freely movable; it measured 2.5 by 2 by 2 centimeters (Fig. 1a).

Microscopic examination of both mucosal masses revealed a similar pattern. The redundant mucosal folds consisted of gastric mucosa composed of gastric glands lined with intact columnar surface epithelium, and chief and parietal cells (Fig. 1b and c). In scattered foci, glandular structures were observed that resembled the pyloric type of gastric gland. The long tortuous gastric glands occasionally showed cystic dilatation deep in the mucosa. Such dilated segments were lined by cuboidal epithelium. The aberrant mucosa was arranged in folds that measured up to 5 millimeters in thickness. Many of these folds contained a thin stalk of loose vascular connective tissue admixed with strands of smooth muscle arising from the muscularis mucosae that followed the larger folds of the mucosal mass (Fig. 1d). At the apexes of the larger folds, glandular structures were seen that in part penetrated the muscularis mucosae and morphologically resembled Brunner's glands.

CASE 2. A 25 year old white woman came to the

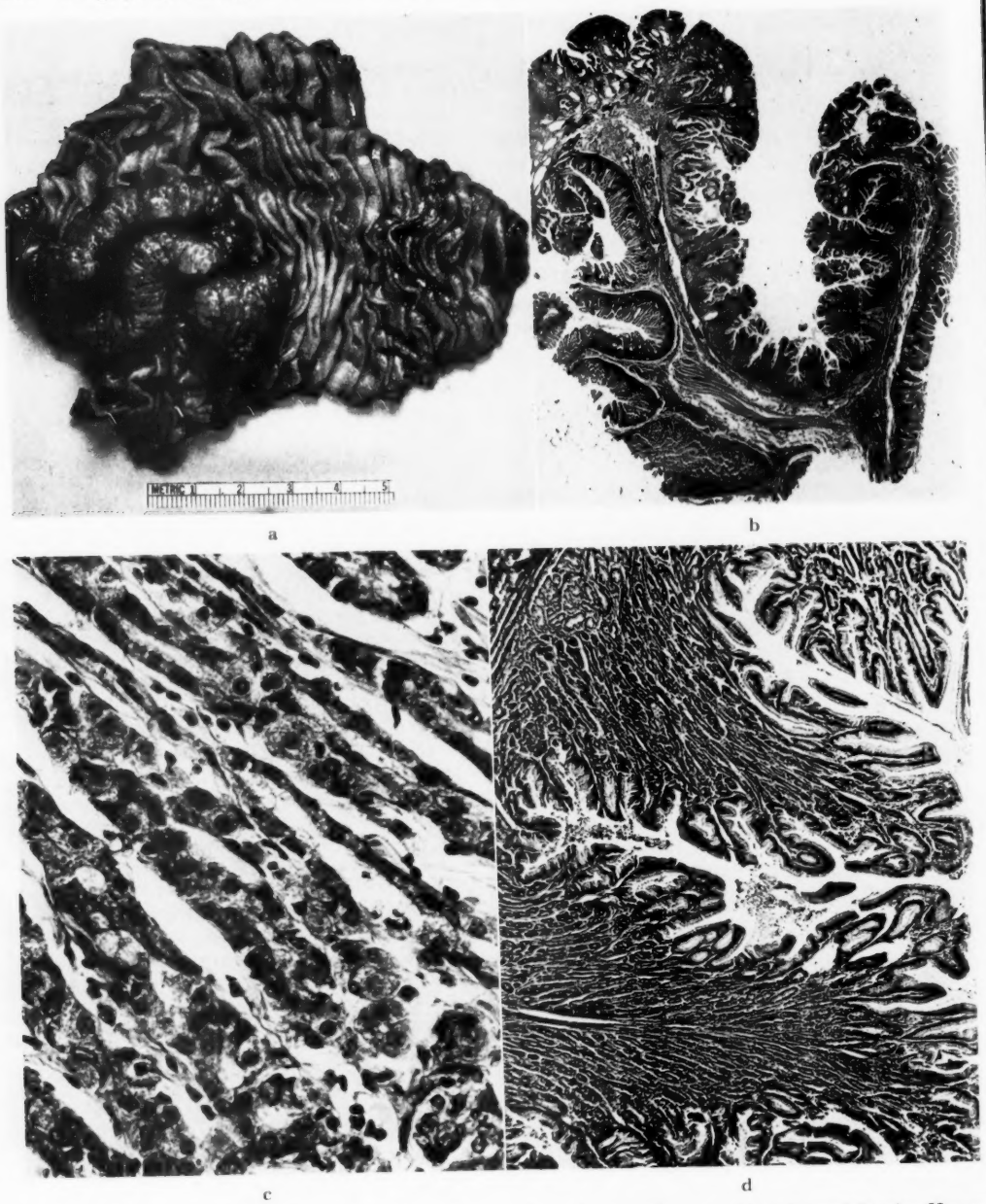


FIG. 1. Case 1. a, The sharply circumscribed, rolled, rugose appearance superficially suggests a villous type of adenoma. b, One of the rugal folds, demonstrating the hypertrophic redundant gastric mucosa, villoid folds, cystic dilatation of the basilar segments of the gastric glands, penetration of glandular spaces into the smooth muscle, and the extensive distribution of smooth muscle. Jejunal mucosa is seen on the extreme right edge. Hematoxylin and eosin, ×3.43. c, The tubular fundic gastric glands contain large numbers of chief and parietal cells. Hematoxylin and eosin, ×343. d, The villoid folds of hypertrophic gastric mucosa exhibit long tubular fundic glands. The villoid fold at the bottom contains a fine strand of smooth muscle. Hematoxylin and eosin, ×32.

clinic in August 1953. Four months prior to registration, she had noted the sudden onset of pain in the left lower quadrant of the abdomen. The pain was crampy in nature and extended across the hypogastrium and around the left flank. Episodes of mild pain were noted almost daily, most frequently after meals. Vomiting was common, particularly when the attacks were severe. The more serious episodes lasted 12 to 24 hours and in some instances required morphine for relief of pain. The patient had noted borborygmi at the peak of the pain on numerous occasions. Neither hematemesis nor melena had been present. Contrast roentgenographic studies of the stomach and colon had not disclosed any abnormalities. Removal of a cyst from the left ovary elsewhere had failed to relieve the symptoms.

Surgical exploration at the clinic disclosed intussusception in the lower portion of the jejunum. The intestine was edematous and its wall was thickened as a result of chronic intussusception. The intussusception was reduced, and a small polypoid tumor was jound to be leading the intussusceptum. A segment of jejunum 6 centimeters in length was resected, and end-to-end jejunojejunostomy was done.

The operative specimen consisted of 6 centimeters of jejunum in the center of which, on the mesenteric border, was a polypoid mass 1.5 centimeters in diameter. The summit of the tumor was ulcerated and the mass was indurated (Fig. 2). Microscopically, the bulk of the polypoid tumor was composed of inflammatory granulation tissue and fibrous tissue secondary to the ulceration. Around the margins of the zone of ulceration, the jejunal mucosa contained islands of gastric mucosa characterized by branched tubular glands that for the most part were lined by tall, columnar, mucous cells. Scattered among the mucous cells were occasional chief and parietal cells. The nature of the inflammatory reaction at the site of ulceration did not suggest peptic digestion and was adjudged to be secondary to the chronic intussusception.

CASE 3. A 6 year old white girl came to the clinic in June 1954 because a mass had been found in the right lower quadrant of the abdomen 3 weeks earlier during a routine physical examination. The child always had been in good health except for a chronic productive cough present since the age of 2.

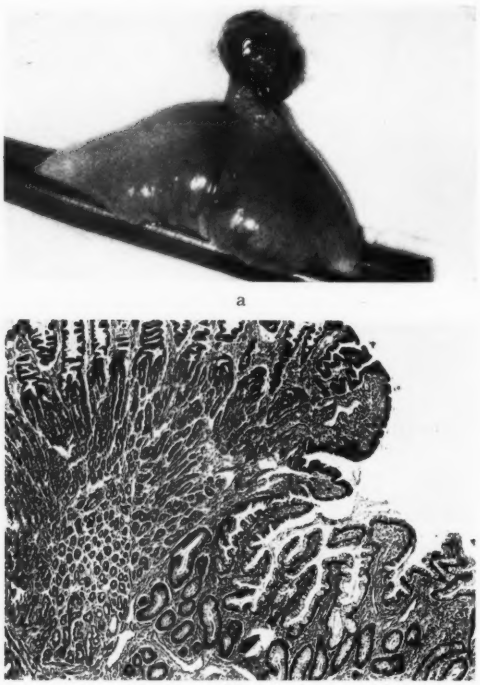
Examination revealed scattered, crackling, wet rales at the bases of both lungs. A moderately firm, nontender, freely movable mass approximately 5 centimeters in diameter was palpated in the right lower quadrant of the abdomen at the level of the iliac crest. Contrast roentgenograms of the small intestine and colon revealed a mass that was thought to involve the cecum and was suggestive of intussusception.

At operation, an intussusception 5 centimeters in length was found 12 centimeters above the ileocecal valve. At the leading edge of the intussusceptum, on the antimesenteric border of the intestine, was a

FIG. 2. Case 2. This small polypoid mass with rather extensive ulceration contained marginal foci of gastric mucosa.

polypoid mass 1.5 centimeters in diameter on a stalk 1 centimeter in length. The tumefaction and a portion of the stalk were removed transileally. The remainder of the small intestine and the colon were normal. The gross specimen consisted of a pale-pink, polypoid mass 1.5 centimeters in diameter situated on a stalk of ileal mucosa 1 centimeter long (Fig. 3a). The mass consisted of redundant folds of mucosa grossly resembling the configuration of an adenoma. Histologically, the mucosa consisted entirely of heterotopic gastric mucosa (Fig. 3b). The gastric glands were lined by parietal and chief cells interspersed with tall, columnar, mucous cells. The stalk consisted of normal-appearing ileal mucosa and muscularis mucosae. The stroma was scanty and consisted of vascular fibrous tissue interspersed with strands of smooth muscle that arose from the muscularis mucosae. The folds of gastric mucosa were tightly packed, which imparted an exaggerated morulation effect not unlike that seen in true adenomatous polyps. Each fold of mucosa contained strands of smooth muscle that interdigitated in an irregular manner with the gastric glands. A mucinous type of epithelium formed glandular spaces in the deeper portions of the mucosa and in some instances penetrated into the smooth muscle in the base of the mass. Dilatation of this type of gland occasionally was seen. Ulceration of the mucosa was absent.

CASE 4. An 11 year old white boy came to the clinic in July 1957 because of attacks of abdominal pain for the past 3 to 4 years. The attacks had been intermittent, occurring on the average of every 2 months



a

b

FIG. 3. Case 3. a, The mass of gastric mucosa on the long stalk of ileal mucosa closely resembles a true adenomatous polyp. b, The sharp transition of ileal to gastric mucosa and the difference in mucosal thickness are demonstrated. Hematoxylin and eosin, ×23.

and lasting from 2½ hours to 2 days. The pain occurred across the midabdomen and was steady and boring. The mother stated that she had seen and felt a mass on the right side of the child's abdomen during some of these attacks. Vomiting usually accompanied the onset of pain. Appendectomy had been done at the age of 6 years for acute perforated appendicitis.

Physical examination disclosed no significant abnormalities. Contrast roentgenograms of the colon revealed a mass in the region of the ileocecal valve that was considered to represent an ileocolic intussusception.

At laparotomy, a 4 centimeter mass was palpated on the mesenteric border of the ileum 45 centimeters above the ileocecal valve. The small intestine for a distance of 15 centimeters distal and proximal to the lesion was edematous and the serosa was thickened from chronic intermittent intussusception. The remainder of the small intestine and the colon were normal to palpation and inspection. A 10 centimeter segment of ileum was resected and end-to-end ileoileostomy was done. At a point 2.5 centimeters above the lower level of resection, the specimen showed an intussuscepting polypoid mass that measured 3 by 3.5 by 0.8 centimeters. The mass was firm and appeared to be covered by redundant folds of mucosa that were freely movable over the surface of the mass, presenting a slightly polypoid plaque (Fig. 4). Microscopically, this plaque of mucosa consisted of gastric glands that were lined by chief and parietal cells and clear, tall, mucous cells. The firm portion of the mass consisted of scanty fibrous stroma and large interdigitating bands of smooth muscle that in part appeared to constitute a portion of the tumor and in part appeared to be secondary to the intussuscepting action of the tumor. While the basic microscopic structure resembled that in Cases 1 and 3, the smooth muscle core was much more prominent. A superficial microscopic ulcer that appeared to be secondary to the mechanical forces of intussusception was found in the adjacent ileal mucosa.

COMMENT

The origin of these masses of ectopic gastric mucosa is open to conjecture. Two concepts have been presented in the literature, namely, that these lesions represent congenital anomalies or that they arise by metaplasia from existing or neoplastic intestinal epithelium.

In 1923, Nicholson wrote in some detail concerning heteromorphosis of the alimentary tract and theorized that such lesions arose by metaplasia from existing intestinal epithelium. Taylor, in 1927, reported 81 cases of all types of epithelial heterotopia of the alimentary tract, dividing them into congenital and acquired types. The latter were less distinct, were associated with chronic ulceration, and were considered to arise by metaplasia. Kimpton and Crane referred to these lesions as an embryonic anomaly but inferred that the potential to develop gastric mucosa probably lay in a pluripotential quality of the intestinal epithelium. They further stated that this pluripotentiality may manifest itself after birth. Gore and Williams considered that the lesion may be explained by metaplasia and hyperplasia in an existing adenomatous polyp.

Metaplasia does not explain the complex cellular elements found in our specimens. It is conceivable that regenerative intestinal

epithelium adjacent to a chronic inflammatory process may produce glandular structures that morphologically resemble the pyloric glands of the stomach. However, when this phenomenon is observed, the cells forming the glands are of the simple columnar type, with varying amounts of mucus. Surface columnar cells of the gastric mucosa and chief and parietal cells do not appear in this regenerative process.

In this respect, it is of interest that Liber did not find any type of cell other than that resembling the cells of pyloric glands in his studies describing aberrant pyloric glands associated with regional enteritis. Morlock and associates were unable to find any evidence of gastric mucosa in 32 cases of primary nonspecific ulcers of the small intestine, nor did they encounter aberrant glandular structures at the edges of the ulcers. The gross and histologic configuration of the mucosal masses in our cases does not simulate that seen in true adenomatous polyps of the small intestine or colon. In Case 3, the long mucosal stalk with the attached mass of gastric mucosa at the tip grossly resembled an adenomatous polyp; however, this was not substantiated histologically. The first and fourth specimens in our series more closely resembled grossly the hypertrophic folds that one finds in the stomach in giant hypertrophy of the gastric mucosa (called Menetrier's disease by Kenney and associates) than they did adenomatous polyps.

The redundant wavy folds in the ectopic mucosa in Cases 1 and 4 presented a rugose appearance and were composed of heterotopic glands containing gastric surface columnar cells, parietal cells, chief cells, and occasional goblet cells. The glandular elements were long and somewhat tortuous; in scattered zones, the basilar portion of the glands presented microscopic cystic dilatation. Fine cores of smooth-muscle cells were frequently observed extending into the mucosa. The muscularis mucosae was continuous with that of the normal mucosa and appeared redundant so as to follow the

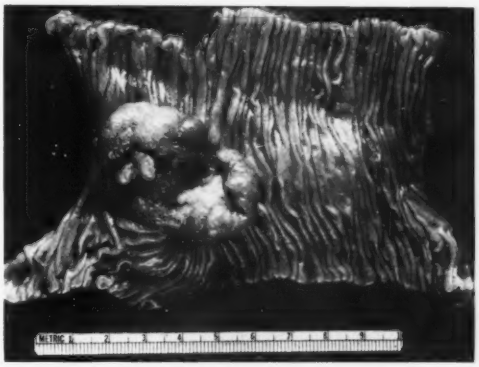


FIG. 4. Case 4. The polypoid configuration of the ectopic mucosa is confined to the surface, and the bulk of the tumor is composed of interlacing bands of smooth muscle, as demonstrated on the cut surface.

mucosal folds of the ectopic masses. In a few zones at the apex of the redundant folds, glandular penetration of the muscularis mucosae was observed. In some instances, these glands resembled Brunner's glands of the duodenum. In other instances, glandular structures were seen that suggested the pyloric type of glands.

The specimen in Case 2 revealed a large zone of ulceration over the surface of the polypoid mass. Narrow marginal islands of gastric mucosa were observed about the periphery. The finding of occasional parietal cells and chief cells in this case would, in our opinion, preclude the possibility that these glands arose secondary to regenerative metaplasia.

The unusual microscopic configuration of these masses of ectopic mucosa and the distribution of smooth muscle strongly resemble the findings in a type of polyp that Bartholomew and associates described in conjunction with the Peutz-Jeghers syndrome. However, none of our patients exhibited mucocutaneous melanotic pigmentation. Because of the admixture of gastric fundic glands, pyloric type of glands, and Brunner-like glands associated with scattered strands of smooth muscle, these lesions more closely resemble hamartomas than true adenomatous polyps. Because of the ectopic

location of these hamartomatous mixtures of tissues, a more precise term would be "choristoma" rather than hamartoma. The ectopic location suggests that these lesions arose from the epithelium of the primitive gut as a congenital anomaly and through hyperplasia slowly increased in size until they attained sufficient bulk to produce intussusception. When one considers the relative frequency of ectopic gastric mucosa in duplication of the small intestine and also in diverticula, as emphasized by Webster, it is not surprising that ectopic gastric mucosa should appear occasionally in an otherwise unaltered segment of small intestine.

The clinical findings in all 4 patients were those of subacute obstruction of the small intestine. Ulceration in 2 specimens probably was caused by chronic intussusception rather than peptic digestion. In 1 instance, the ulceration was acute and superficial and was confined to the ectopic mucosa, whereas the ulceration in the second instance involved much of the polypoid mass of aberrant mucosa that represented the leading edge of the intussusceptum. As already mentioned, however, Taylor described a small ulcer in the ileal mucosa adjacent to ectopic gastric mucosa in a young child that may have been secondary to peptic ulceration from gastric juices. As in the case of diverticula, one would expect to find peptic ulceration involving the adjacent normal mucosa rather than the aberrant mucosa.

SUMMARY

A clinical and pathologic study was made on 2 children and 2 young adults seen at the Mayo Clinic who had masses of polypoid ectopic gastric mucosa in the small intestine that resulted in subacute partial obstruction of the small intestine secondary to intussusception. Reports of 6 similar cases were found in the literature.

In 3 of the present cases, the gross and microscopic findings indicated that these lesions are composed of a hamartomatous mass of ectopic gastric mucosa. One specimen exhibited extensive ulceration of the mucosal mass that appeared to be secondary to chronic intussusception and contained only remnants of gastric mucosa.

Three types of specialized cells of the gastric mucosa were demonstrated in all 4 cases, which precludes origin from metaplasia of existing intestinal mucosa. In no instance was peptic ulceration associated with the ectopic tissue.

Treatment consisted of segmental resection and end-to-end anastomosis in 3 cases and local transileal excision in 1 case.

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CONGENITAL DEFICIENCY OF THE ABDOMINAL MUSCULATURE AND OBSTRUCTIVE UROPATHY

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THE LIFE-THREATENING SYNDROME of congenital deficiency of the abdominal musculature and obstructive uropathy can be recognized at a glance provided the observer is familiar with the disorder. The obvious deficiency in the abdominal wall is the unmistakable sign of the syndrome, but the hidden urinary deformity is its potentially death-dealing component. The characteristic appearance of the abdomen can be noted at birth. However, whether noted at that time or later in life, prompt evaluation of the urinary tract is imperative to intelligent therapy. Proper treatment varies, but early death can be averted in at least some instances. Though a survey of the literature reveals fewer than 100 cases, the reported incidence may increase as information about the disorder is more widely disseminated and with greater understanding that there is some therapeutic hope. Case 1 is presented in some detail because it characterizes the rather advanced stage commonly encountered, reveals what we currently believe is the proper management, and demonstrates that a good result can be obtained at times.

CASE REPORTS

CASE 1. C. E. was a boy, born of the second uncomplicated pregnancy of a 37 year old mother whose blood group was B, Rh positive. His brother was normal. Immediately upon delivery the abdomen was noted to be flabby, wrinkled, and to flop about under the influence of gravity. Intestinal activity could easily be observed beneath the intact but obviously thin abdominal wall. Although the musculature of the abdomen was hypoplastic, the greatest degree of deficiency appeared in the lower right quadrant, and the least in the upper left. A flare of the costal margins with Harrison's groove above was also evident. The penis was well formed but the testes could not be identified. No other anomalies commonly associated with the syndrome, including those in the lower extremities, were present. Urine obtained at the first and second voidings contained a few red cells but no pus cells or albumin. Urologic consultation was promptly requested. The blood urea nitrogen was 16 milligrams per cent. The phenolsulfonphthalein (P.S.P.) output from the bladder in 3 hours was only 16.5 per cent, but the specimens were not collected through a catheter at this time. A urethral catheter passed easily and a cystogram made at 15 to 20 centimeters of water pressure revealed a large, irregular bladder which appeared to be attached to the abdominal wall in the region of the umbilicus. The cystogram also demonstrated bilateral ureteral reflux into large, coiled ureters (Fig. 1). Therapeutic procrastination was occasioned by our inexperience and abetted by the normal blood urea nitrogen and the absence of pyuria.

On the twenty-first day, bilateral nephrostomy was carried out under local anesthesia. In spite of the dilated pelves, the renal parenchymas appeared healthy and averaged about 1 centimeter in thickness. Six days later pyeloureterograms were made through the nephrostomy tubes at a pressure of 20 centimeters of water, using one of the standard media employed for intravenous pyelography (Fig. 2). On the thirtieth day of life the P.S.P. excretion in 3 hours was 35 per cent from the right nephrostomy and 31 per cent from the left.

On the forty-ninth day of life the left ureter was straightened through an extraperitoneal approach. In making the abdominal incision, only rudimentary, nonfibrous, platysma-like muscles were encountered. An excessive length of 9 centimeters was excised from the lower end which was then reimplanted into the base of the bladder using a tunnel and fishmouth technique. Catheterization and roentgenograms revealed that the ureter was actually straight. The vesical outlet did not appear definitely abnormal, but at this time we were not keenly aware of the probability of an obstruction here, so the examination cannot be considered adequate. However, later follow-up has

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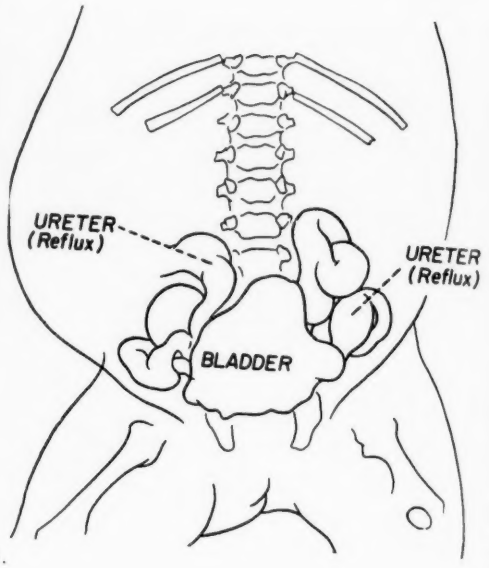

FIG. 1.

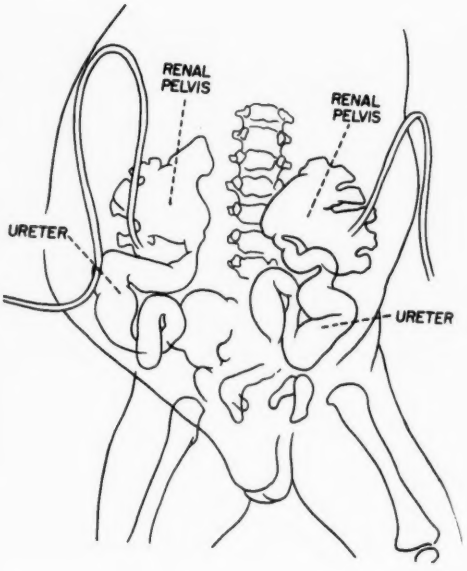

FIG. 2.

FIG. 1. Case 1. Preoperative gravity cystogram demonstrating a large, irregular bladder and bilateral ureteral reflux. Left, Exposed x-ray film; right, phantom drawing.

FIG. 2. Case 1. Pyeloureterogram made through the nephrostomy tubes, on the twenty-seventh day of life.

indicated that any abnormality here was minor in degree. Histologically, the excised portion of the ureter showed the changes of chronic ureteritis with fibrosis and hypertrophy of the muscle coats. Nerves were easily identified in the specimen, but not the ganglion cells. A febrile episode caused by malfunction of the right nephrostomy delayed a similar operation on the right ureter until the sixty-eighth day of life. Study of the excised portion of the lower right ureter after staining by the Cajal method showed small nerve bundles accompanying the blood vessels as well as nonmedullated nerves running into the muscle bundles. The patient progressed satisfactorily. The recordings of the pressures through the nephrostomy tubes (while they were attached to a burette in a manner similar to that used in testing choledochal drainage through a T tube) have been lost, but we recall that both pressures were less than 10 centimeters of water. A cystogram revealed mild reflux up the right ureter but not up the left. The catheter in the left nephrostomy was removed 36 days after the straightening of the left ureter, and the right, 28 days after the procedure on the right ureter. Both nephrostomies closed promptly.

The patient was discharged at the age of 5 months with a functioning cystostomy and, for the first time, was wearing an abdominal binder for support. Our plan was to observe the outcome of these procedures for some months while the influence of a possibly complicating but unrecognized obstruction at the vesical outlet was held in abeyance by the cystostomy drainage. At the age of 1 year, the following items were noted: the urine was infected; the blood urea nitrogen was 13 milligrams per cent; the P.S.P. output was 60 per cent in 2 hours; the urea clearance was 32.4 and 23.1 per cent of adult normal; intravenous pyelography demonstrated fair function in 10 minutes, bilaterally; a cystogram revealed a mild left ureteral reflux with a nearly normal pyelogram and a straight but mildly dilated ureter, with no reflux up the right side; and the residual urine in the bladder after voiding with the cystostomy tube clamped was 20 cubic centimeters. A month later there was further evidence of improved renal function (total P.S.P. output was 94 per cent in 2 hours) and the cystostomy catheter was removed. Generally, the patient progressed satisfactorily but, from time to time, drainage from the cystostomy site would occur and consequently he was readmitted at the age of 3½ years. On this admission the urine was sterile, intravenous pyelography disclosed no essential change, and the cystourethrogram revealed no ureteral reflux. The vesicocutaneous fistula was excised and successfully closed. Since that time the patient has been seen on numerous occasions and has thrived (Fig. 3). He wears an abdominal support and is active in sports. Bowel function remains normal. At the age of 10 years a left orchiopexy was performed. The testis was intra-abdominal and no hernial sac was found. A testicular biopsy disclosed a mild hypoplasia, no different from that expected in ordinary cases of cryptorchism. Results of urinalyses were negative and a culture of the urine was sterile. The blood urea nitrogen was 14 milligrams per cent, and the P.S.P. output 100 per cent in 2 hours. Intravenous pyelography (Fig. 4) demonstrated prompt function and reasonably satisfactory architecture. The large bladder was again noted by cystourethrography, but the residual urine was only 20 cubic centimeters (Fig. 5).

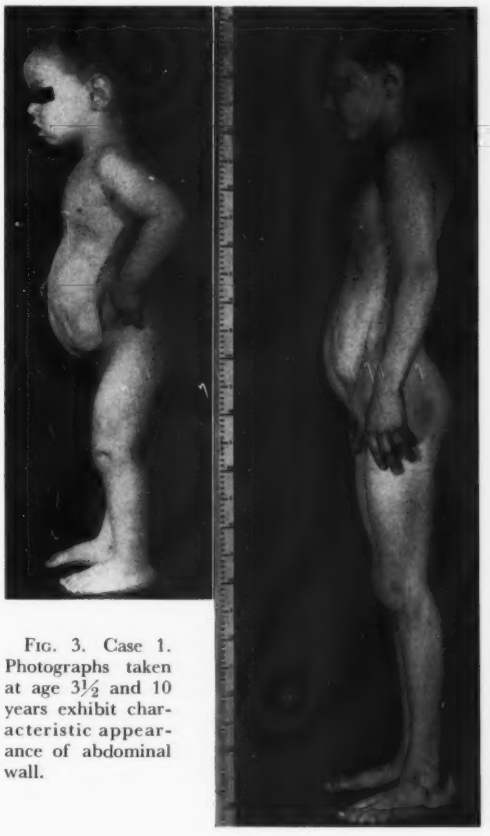

FIG. 3. Case 1. Photographs taken at age 3½ and 10 years exhibit characteristic appearance of abdominal wall.

The syndrome has varied much in degree but little in type. Sometimes the deficiency in the abdominal musculature has been limited to one quadrant, but at other times the whole anterior abdominal wall and parts posterior have been affected; for example, in Case 6 the quadratus lumborum was also absent. The muscular inadequacy may impair respiration, and fatal pulmonary infections have not been rare. The thin, inactive

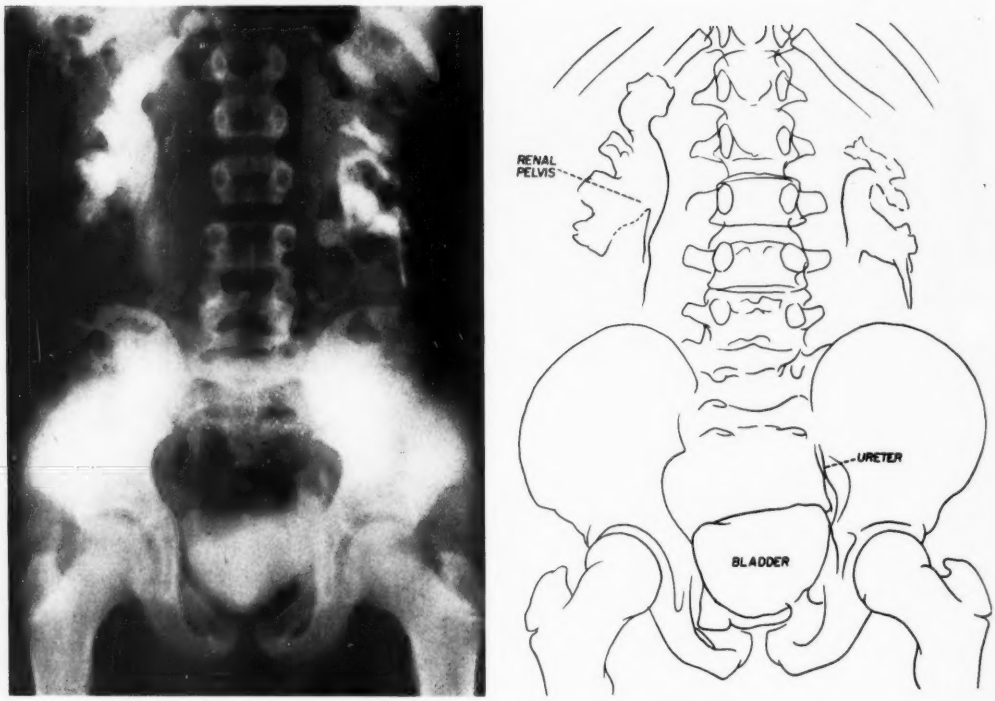

FIG. 4. Case 1. Intravenous pyelogram at age 10 years.

abdominal wall causes a characteristic appearance like that of a flabby sack, through which the intestinal movements can be noted. The skin tends to be wrinkled, suggesting the exterior of a dried peach or prune (the affliction has been nicknamed "the prune belly syndrome"). Most commonly bilateral cryptorchism has been present, but on rare occasions both testes have been descended; for example, 2 of Lattimer's 20 male patients had bilaterally descended testes. The syndrome has been quite rare in female patients, only 4 or 5 instances having been reported. Coexistent anomalies apart from those in the genitourinary tract and the abdominal wall have been very frequent. About one-fourth of the patients have had deformities in the gastrointestinal tract, and these have occasionally caused clinical problems during infancy. In addition to the deformity of the lower thoracic cage with Harrison's groove, other thoracic anomalies have been common, particularly pigeon breast. Abnormalities of the lower extremities have been frequent. Such anomalies were present in 12 (29 per cent) of the 42 cases collected by Metrick and associates (half of these 12 being of the clubfoot variety), in 41 per cent of Lattimer's series, and in 29 per cent of our small group. Coexistent cardiovascular anomalies have been infrequently reported except that 8 of Lattimer's 22 patients had demonstrated or suspected peculiarities in this system. No cardiovascular anomaly was detected in any of our 7 patients including the 2 on whom autopsies were performed.

The truly serious feature of the syndrome is the obstructive uropathy. Most of the deaths have been caused by renal deficiency and urinary sepsis. The mortality in the first few years has been high. Three of our 7 patients died in early infancy, and 7 of Lattimer's 22 patients died within 12 days o

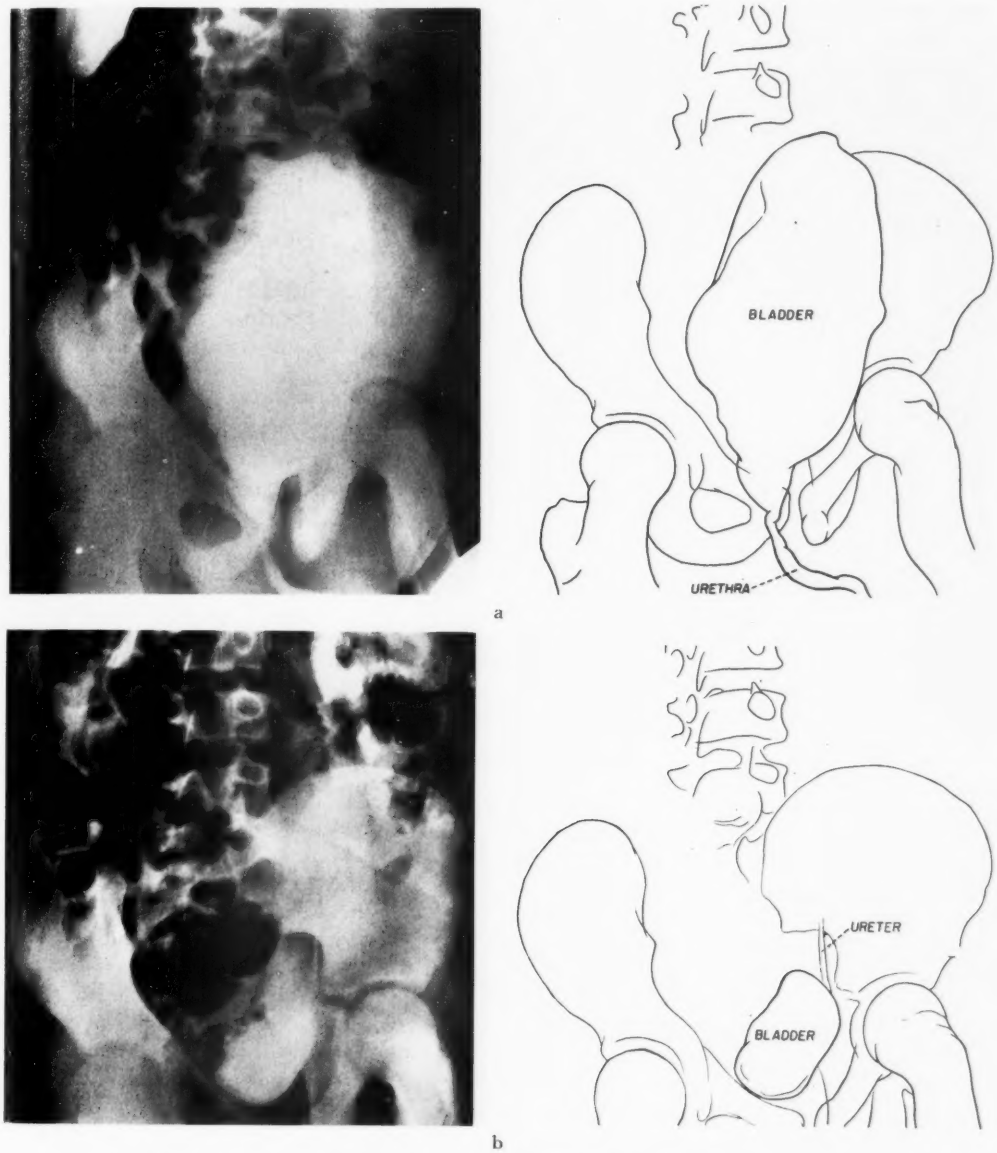

FIG. 5. Case 1. a, Voiding cystourethrogram demonstrating a large bladder and normal appearing urethra. b, Postevacuation cystourethrogram demonstrating mild left ureteral reflux and small residual.

birth because the urinary tracts were already damaged beyond salvage. The characteristic deformity has been hydronephrosis with severe dilation and extreme elongation of the ureters; but in some cases the degree of hydronephrosis proper has tended to be less than one would expect from the change in the ureters. The urinary bladder has usually been large and thick-walled and at times deformed in an hour-glass shape. Patent

FIG. 6. Case 2. Photograph at birth exhibits the characteristic appearance of the abdominal wall.

urachus has been frequently present, as in Case 3, but classical exstrophy of the bladder has not accompanied any of the reported cases. Characteristically, cystography reveals ureteral reflux, and delayed films demonstrate poor emptying of the ureters with the obstruction at the ureterovesical junction. Obstruction at the vesical outlet has varied much in degree, but some is probably present, even though this has not always been demonstrated conclusively by current methods. There is a real possibility that the patient in Case 1 could have been, and might still be, improved by plastic revision of the vesical outlet.

Etiologically, this compound anomaly obviously has an embryologic background. It has been suggested that the primary deficiency is of the abdominal wall and that the lack of compression permits the urinary distention. If this were true, the degree of change in the urinary tract should closely correspond to the degree of abdominal inadequacy, but actually this correlation has been merely general. In a few instances, the abdominal wall has been quite flabby yet the urinary tracts have not been dilated. Patients with huge abdominal hernias, including congenital omphaloceles, do not regularly have hydronephrosis and large bladder. Furthermore, since the abdominal pressure is evenly distributed the changes in the upper urinary tracts should be approximately equal in the individual patient, but such equality has clearly not existed in several reported cases. At least 1 attempt, reported by Riparetti and Charnock, has been made to manage the disorder by providing support through plastic revisions of and fascial transplants into the abdominal wall. The follow-up in this case has been incomplete, but the child was leading an active life 22 months after discharge, although he had had "minor urinary infections" and 1 episode of pneumonitis.

The hypertrophied bladders usually found in these cases bespeak obstruction rather than passive distention. As might be expected, another suggested theory is that the primary difficulty is an obstruction within the urinary tract, so that as it decompensates and dilates, pressure produces the deficiency of the abdominal wall. The probably high incidence of some degree of vesical outlet obstruction lends support to this theory, as does the hypertrophy and large volume of the bladder in most cases. However, urinary tract dilatation as the result of obstruction, while common enough even in the newborn, is not ordinarily associated with deficiency of the abdominal musculature and, as already mentioned, there have been instances of the abdominal deficiency without distention of the urinary tract. The position of the deficiency in the abdominal musculature has frequently been removed from the site of direct pressure by the distended bladder, and it is difficult to account for the well documented examples of localized or unilateral deficiency. The gross and

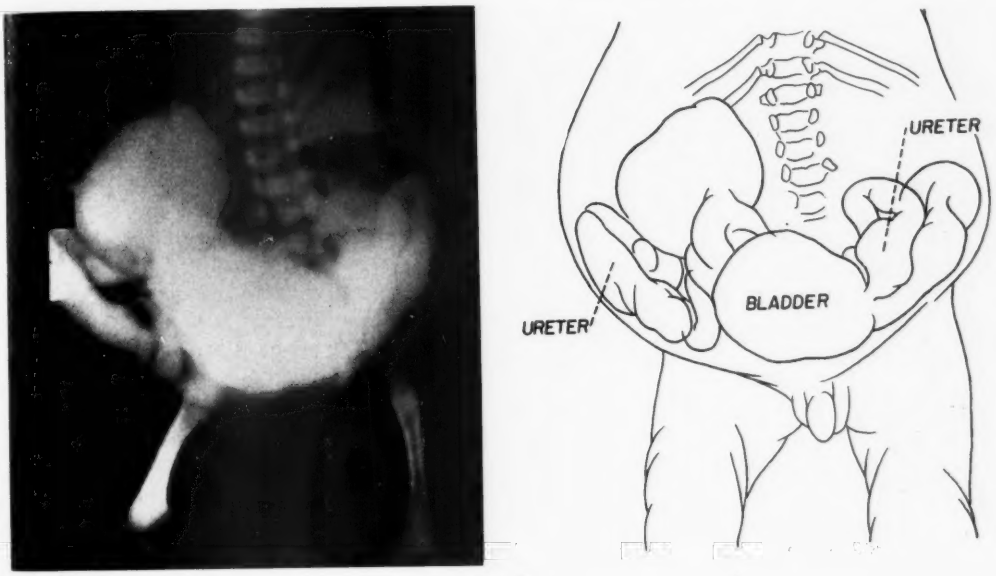

FIG. 7.

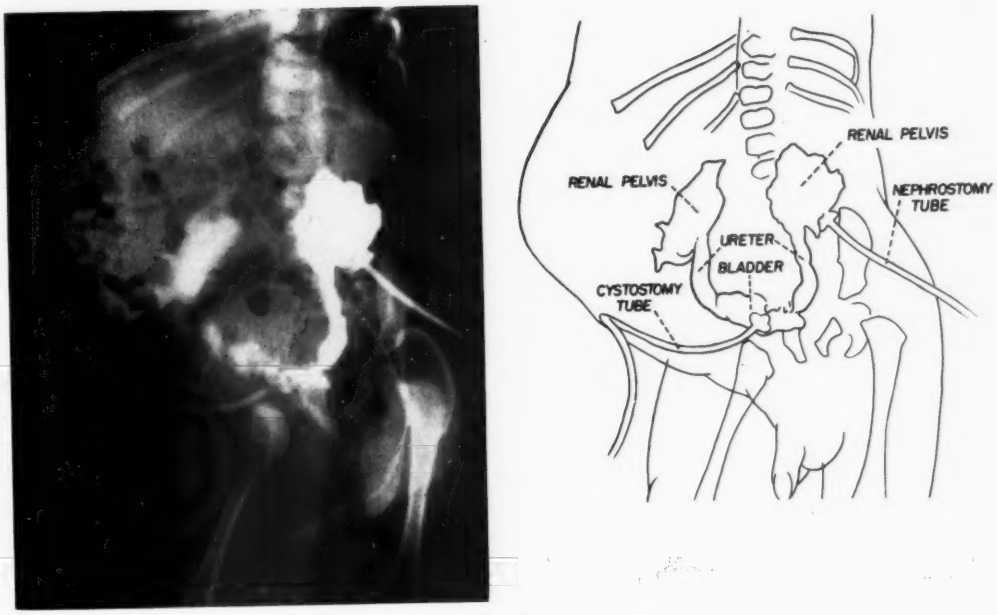

FIG. 8.

FIG. 7. Case 2. Cystogram performed via urethral catheter demonstrating bilateral ureteral reflux, bilateral hydronephrosis, and hydroureter.

FIG. 8. Case 2. Retrograde pyelogram performed through the left nephrostomy tube demonstrates straightened ureters with reflux on the right.

FIG. 9. Case 3. Roentgenogram of feet showing rudimentary toes and bilateral talipes equinovarus.

even histologic examination of the abdominal wall does not suggest an atrophy, but rather a severe hypoplasia. Finally, neither of these 2 etiologic speculations would account for the very frequent coexistent anomalies at a distance from the abdominal wall and the urinary tract, especially the frequent deformities in the lower extremities. Since no 2 cases in the same family have been reported, it is unlikely that the syndrome is hereditary. It seems more likely that some deficiency affects the whole fetal development at some early time, particularly altering structures simultaneously at a crucial stage.

As is so common with idiopathic disorders, a neurogenic causation has also been postulated. Mental deficiency and recognized congenital neurologic disorders have been notably absent in the reported cases, but a brain disorder was found at autopsy in Case 2. The spinal cords of 4 patients were carefully examined by others, and no evidence of poliomyelitis or defect was found. The possibility of an intramural nerve defect of the type indicated by Swenson in congenital megacolon might be considered. If so, the defect would certainly have to be diffuse to affect both the urinary tract and the abdominal wall, and yet, not affect the best known site, the colon (only 1 example of coexistent megacolon was found in the literature). In Cases 1, 3, 4, and 7 apparently normal nerves were found in the excised portions of the lower ureters. The occasional therapeutically excellent results, even in severe cases, appear to have been achieved by mechanical alterations that would not seem to have wrought an improvement in nervous factors. In short, we

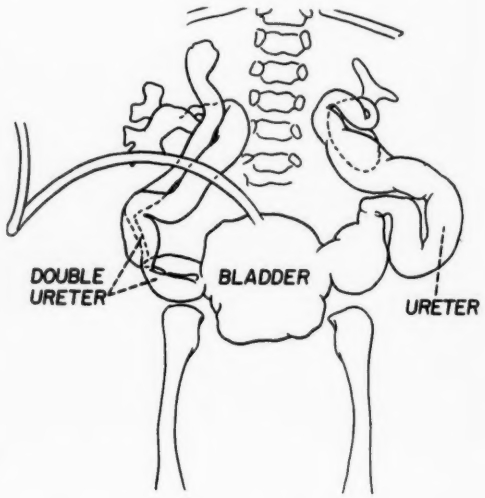

FIG. 10. Case 3. Cystogram performed via the vesicocutaneous fistula. Bilateral hydronephrosis and hydroureter are demonstrated.

incline toward a causation based on general embryologic deficiency rather than on a primary deficiency localized either to the urinary tract, the abdominal wall, or the nervous system.

Management should begin with immediate recognition that the syndrome is present and with prompt evaluation of the urinary tract. The kidneys have often been irreparably damaged at birth, and the ever-impending infection may be present then (Case 2). In the mildest deformities surgical drainage may not be required, or at least may not be necessary as an emergency measure—but the burden of proof lies on the surgeon who does not provide it. In our opinion, the fact that a few patients have survived months, and occasionally even years (Case 7), without fundamental therapy is more a tribute to their good fortune in starting with fairly good kidneys and semiadequate elimination

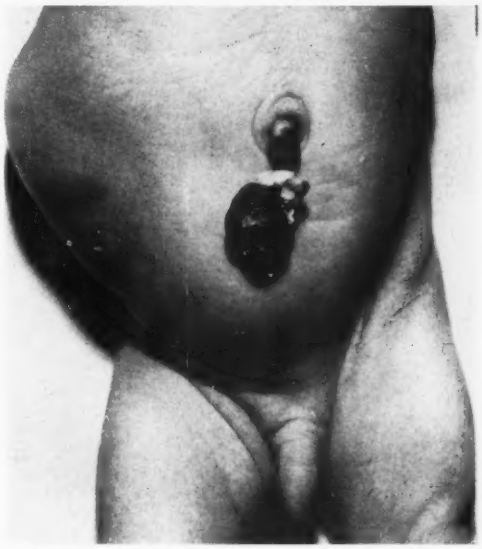

FIG. 11. Case 4. Photograph of abdominal wall shortly after birth disclosing the characteristic deformity.

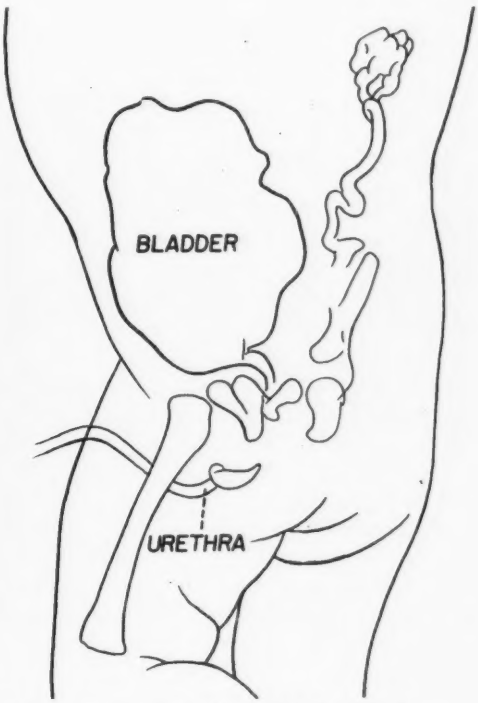

FIG. 12. Case 4. Cystourethrogram demonstrating a large irregular bladder with left ureteral reflux.

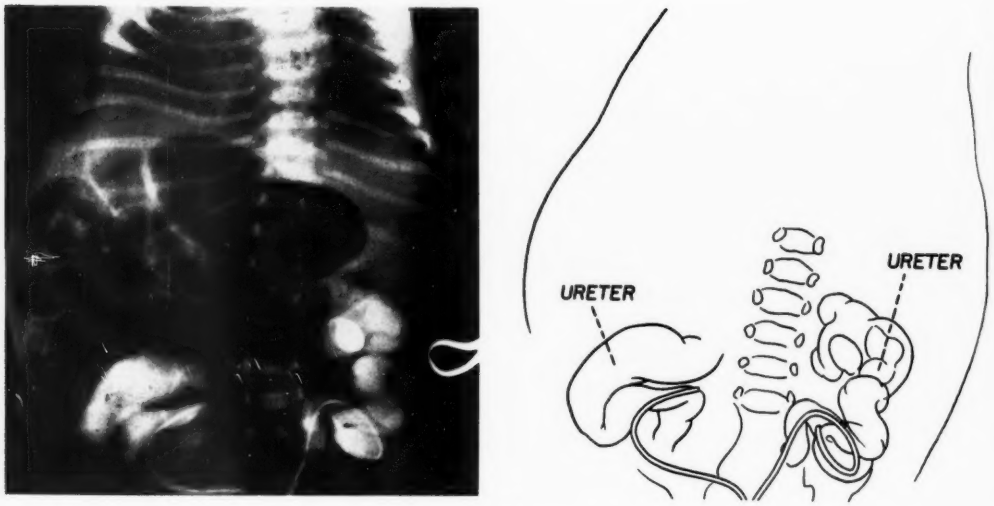

FIG. 13.

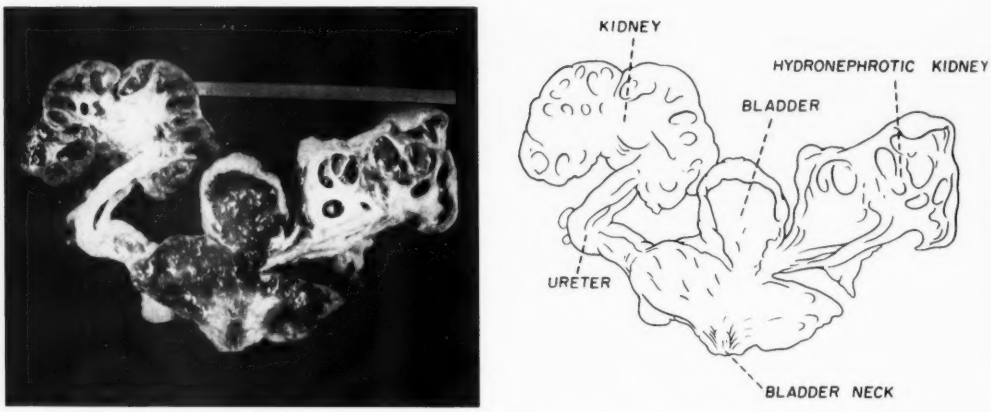

FIG. 14.

FIG. 13. Case 4. Retrograde pyelogram performed via exploratory cystotomy. Markedly dilated and tortuous ureters are noted.

FIG. 14. Case 4. Autopsy specimen showing extreme destruction of renal parenchyma. The left ureter had been straightened and reimplanted into the bladder.

than an argument for "masterly inactivity." A normal blood urea nitrogen and a clear urine may permit some little delay, but the renal compensation is often barely marginal even in the face of these hopeful signs. Cystography has usually been the most valuable diagnostic test. The patient has been simply and gently catheterized with a small catheter and the bladder filled to capacity at a pressure of approximately 15 centimeters of water. Reflux into the upper urinary tracts has been usual, so that pyeloureterograms were also obtained. Exposures made at intervals after the filling usually provided evidence of multiple sites of obstruction, particularly at the ureterovesical junctions. A urethrogram may be made if convenient, but this has not seemed

essential at this stage. Of course, intravenous pyelography may be useful but function has frequently been so reduced that films 4 or more hours after the injection have been required to show architectural detail. Although cystoendoscopy in the male newborn is possible, there are very significant hazards, especially to the urethra. Accordingly, an exploratory cystotomy with ureteral catheterization and retrograde pyelography (Case 4) may be safer when cystography and intravenous pyelography fail to deliver the needed information.

When there is sufficient abnormality to justify surgery, and there usually is, we believe bilateral nephrostomy to be the most desirable first fundamental step. Although good results have been obtained without the use of nephrostomy, immediate fatalities have also been caused by neglecting this procedure (Cases 3 and 4). The emotional and sympathetic pressures on the surgeon managing a serious urologic disorder of an infant can warp judgment only too easily. Generally speaking, nephrostomy is the procedure most likely to divert the urine above any gross obstructions, mechanical or functional. Local anesthesia has usually sufficed, since the hydronephroses have commonly been large and easily tapped. Of course, general supportive measures and urinary antiseptics are valuable adjuncts in the program. Ideally, the nephrostomies should be maintained until the maximal return of renal function has appeared. In practice, compromises may have to be made; for example, pocketed infections in the ureters or bladder may require specific attention.

The next procedure that we believe is usually advisable is careful straightening of the ureters with excision of excessive length and reimplantation into the base of the bladder. Operating upon each ureter at a separate session has seemed conducive to a desirably meticulous dissection. In our cases, the excess was removed from the lower end of the ureter and the reimplantation was carried out by a tunnel and fishmouth technique (Cases 1 and 2) or by a tunnel and cuff technique (Cases 3 and 4). While it may be possible to thread a catheter through kinks in the ureter in an upward direction, downward flow may still be grossly impeded. Therefore, pyeloureterography in the operating room at the completion of the reimplantation has been valuable in detecting angulations in the ureter not otherwise evident.

FIG. 15. Case 5. Photograph of infant exhibiting characteristic abdominal wall.

After a period of 2 or 3 weeks, the circumstances have usually been appropriate for a detailed re-evaluation. Pyeloureterograms can be made through the nephrostomy catheters and the presence or absence of reflux determined by cystography via the suprapubic catheter. The nephrostomies may be attached to a burette to observe the drainage pressures. In our experience, if the pressure without abdominal straining has remained at 10 centimeters of water or less, and blue colored fluid runs from the burette down and out the cystostomy opening, the result of this portion of the effort has been

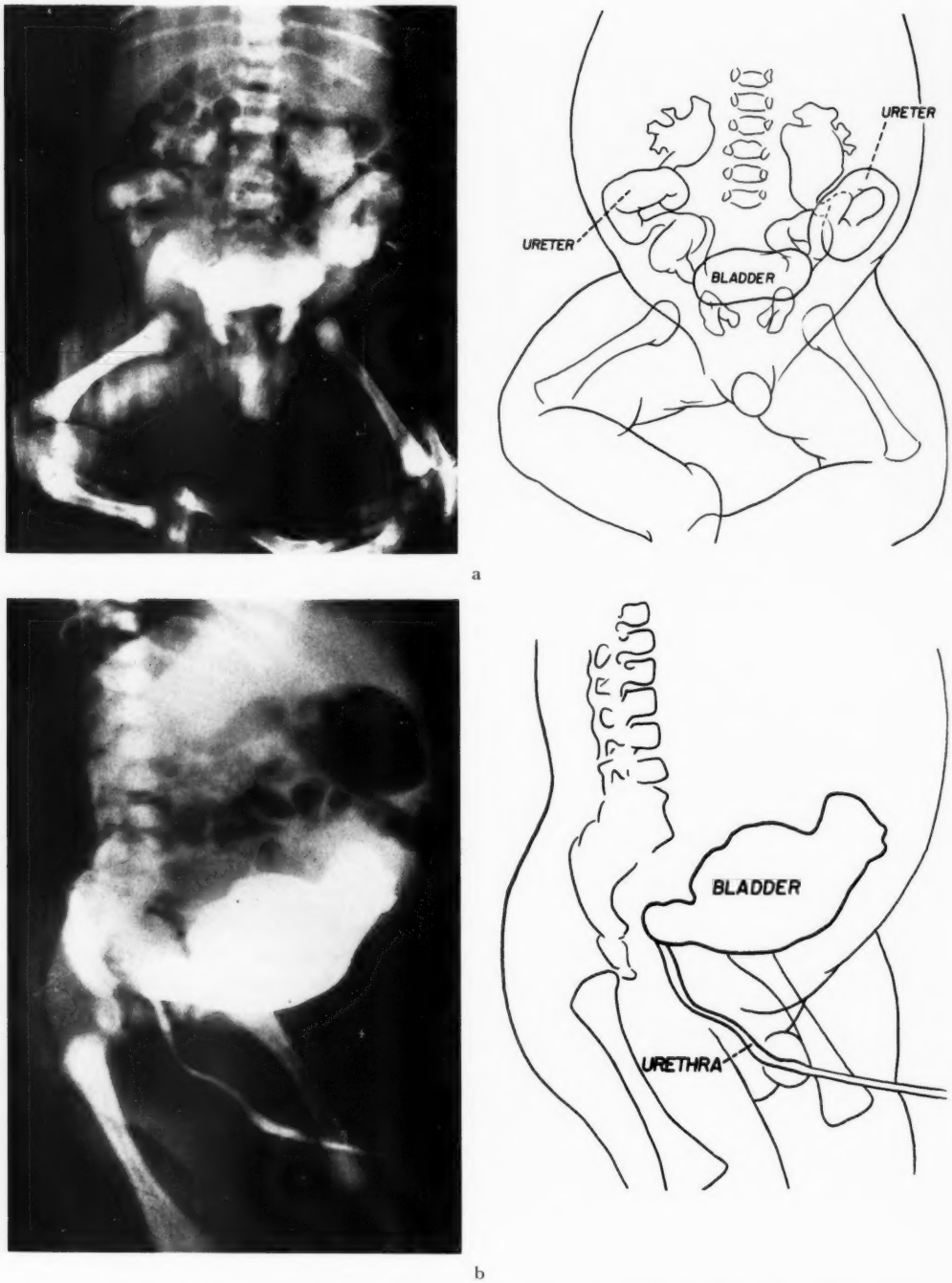

FIG. 16. Case 5. a, Gravity cystogram demonstrating bilateral ureteral reflux with bilateral hydronephrosis and hydroureter. b, An injection cystourethrogram, shows a large irregular bladder.

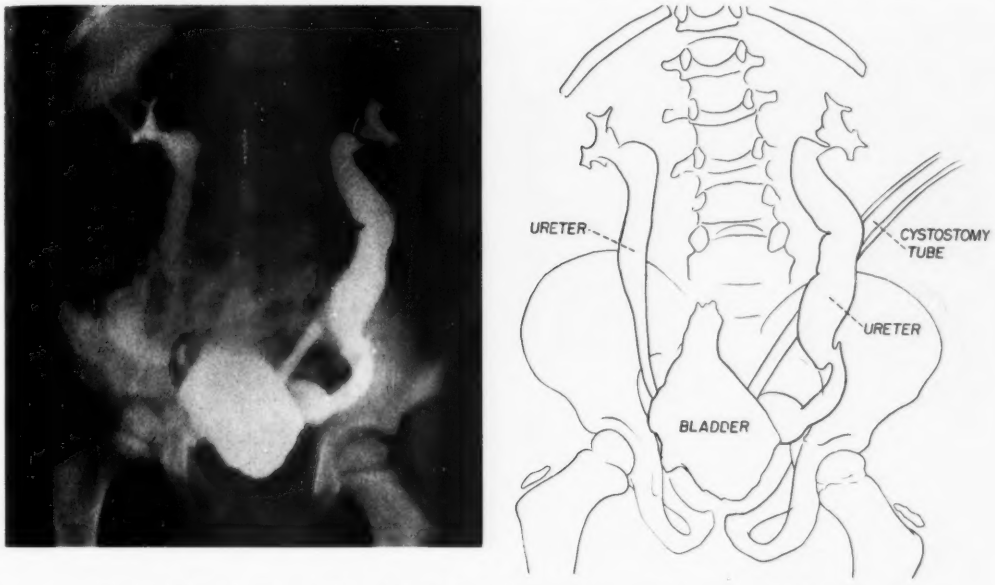

FIG. 17. Case 6. Cystogram performed through the cystostomy tube demonstrating bilateral ureteral reflux.

good. Pressures of over 15 centimeters have almost invariably indicated inadequacy, although a further wait for inflammatory induration to subside may provide more favorable signs. The testing of one side at a time seems logical since febrile reactions have not been rare. When these indications were favorable, the renal tubes have been removed at separate times. The cystostomy is probably best maintained for about 6 months and then the whole situation evaluated once more. If the upper urinary tracts have remained satisfactory, any deterioration in them subsequent to the closure of the cystostomy opening would most probably reflect an inadequacy in the lower tract which then demands attention.

Gross deformities of the bladder can usually be corrected when it is first opened. At some convenient time, urethrography and palpation of the vesical neck should be done. Anterior Y-V plasty of the vesical outlet or plastic V-wedge excision of the base of the vesical neck has not been invariably necessary (Case 1), but our present tendency is toward such a revision on what we would have considered only slight indication a few years ago. In most cases, we have preferred open surgical plastic revision of the vesical outlet to transurethral resection. If it should be decided that the vesical outlet is now adequate, with or without surgery, the cystostomy can reasonably be removed. Every effort should be expended to clear up any residual infection and the patient should be closely followed for the first year even if all evidence continues favorable.

The following reports are résumés of our other 6 cases of this syndrome of congenital deficiency of the abdominal musculature and obstructive uropathy.

CASE 2. M. K., was the product of the third, apparently normal pregnancy of a 27 year old mother whose blood group was A, Rh positive. The patient's brother, sister, and 1 sibling born subsequently have no recognized congenital defects. The characteristic appearance with bilateral cryptorchism and bilateral clubfoot was noted at birth (Fig. 6). The first voided urine was cloudy, and the specimen examined 12 hours after birth contained albumin (2+), innumerable white blood cells, and Aerobacter aerogenes. Evidently, the patient had pyuria and infection at

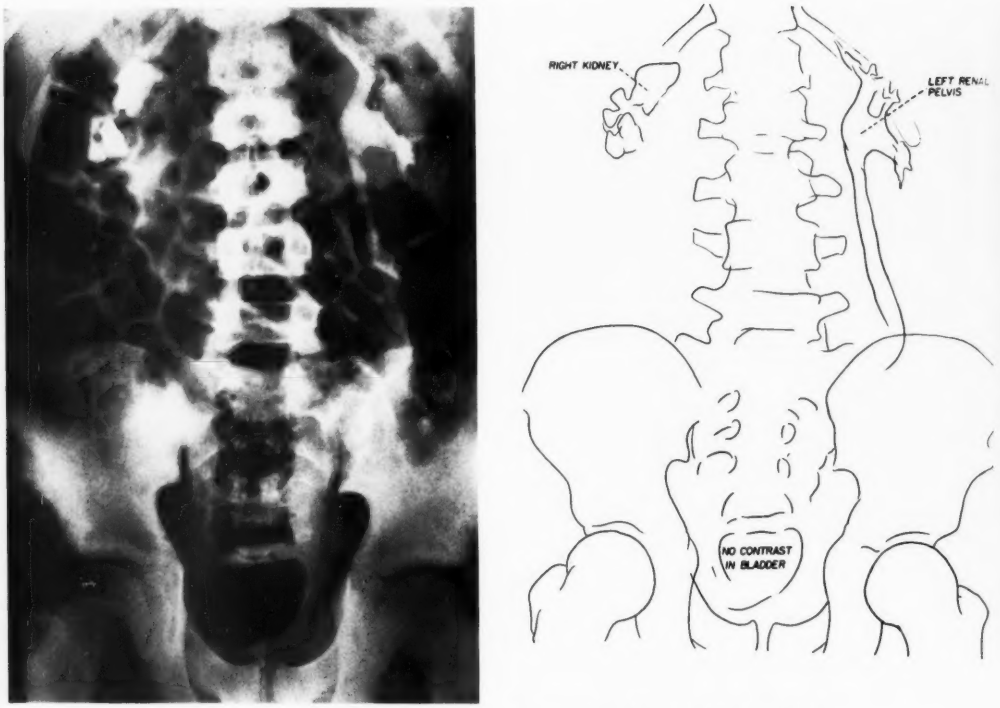

FIG. 18. Case 7. Intravenous pyelogram demonstrating bilateral hydronephrosis.

birth. On the second day of life, cystography indicated a large bladder, bilateral ureteral reflux, bilateral hydronephrosis and hydroureter, and no definite calyceal patterns (Fig. 7). Intravenous pyelography did not reveal function up to 80 minutes following injection. On the third day of life, exploratory cystotomy, bilateral ureteral straightening, and reimplantation with tunnel and fishmouth technique, and bilateral nephrostomy were performed under general anesthesia. The renal parenchymas were each about 6 millimeters thick. The vertical incision just to the right of the midline revealed only a thin layer of opaque fascia and some transverse muscle fibers less than 1 millimeter in thickness between the skin and the thick vesical wall. The pressure in the bladder varied between 15 and 21 centimeters of water. The widely patent ureteral orifices were each 1 centimeter behind the tremendously hypertrophied trigone. The 18 centimeters of excised ureter averaged 1½ centimeters in diameter, and histologically there was evidence of chronic ureteritis and at least a few nerves could be identified. The blood urea nitrogen reached 106 milligrams per cent on the ninth postoperative day, accompanied by acidosis. Under intensive therapy, the blood urea nitrogen gradually dropped to 22, but it did tend to rise under the slightest stress. Pyelographic studies indicated that both ureters were straight and patent (Fig. 8). Drainage pressure measured through the right nephrostomy tube was rarely above 4 centimeters of water, and that on the left remained in the general region of 8 centimeters. The nephrostomy tubes were separately removed and the sites healed promptly. The infant then gained weight, appeared generally better, and was no longer a severe metabolic problem. However, cystography through the suprapubic tube did reveal persistence of bilateral ureteral reflux. At the time of discharge with the functioning cystostomy, the urea clearance was 21 per cent of normal. The child progressed slowly at home but had no major difficulty until there was a rather sudden deterioration at the age of 8 months and he died. Postmortem examination was performed elsewhere and was reported as showing bilateral hydronephrosis and hydroureter with infection, absent left testicle, intra-abdominal but otherwise normal right testicle, and a degenerative disorder of the brain with porencephalia, destruction of myelin, and sclerosis. While it cannot be said that the relief of the urinary obstruction-infection was ideal, the studies did indicate a significant improvement. Apparently the renal destruction was too advanced at birth to be amenable to correction.

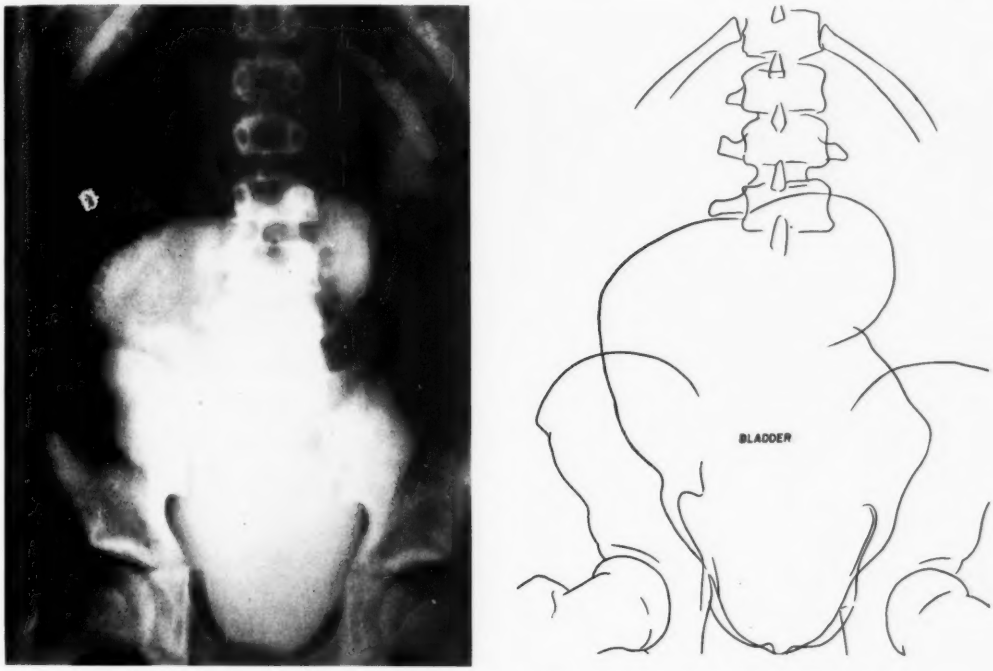

FIG. 19. Case 7. Cystographic study demonstrating a large irregular bladder without ureteral reflux.

CASE 3. K. J., was admitted at the age of 3 months for the evaluation of congenital anomalies. He was the product of the apparently normal first pregnancy of an 18 year old Negro mother. At birth the characteristic appearance with bilateral cryptorchism and a vesicocutaneous fistula at the umbilicus was noted. He failed to progress satisfactorily. Intravenous pyelography elsewhere had revealed bilateral hydronephrosis. The blood urea nitrogen had ranged between 17 and 24 milligrams per cent. The urine continued to be infected in spite of intensive antibiotic therapy. Bilateral dislocation of the hips and bilateral talipes equinovarus with rudimentary toes were also present (Fig. 9). A catheter was inserted into the bladder through the vesicocutaneous fistula (patent urachus) and cystography demonstrated the presence of bilateral ureteral reflux with hydronephrosis and hydroureter (Fig. 10). Drainage was poor through the ureterovesical junctions. The left kidney was noted to be small. The urea clearance was 46 and 42 per cent of normal and the P.S.P. excretion, 10 per cent in 20 minutes via a catheter inserted into the bladder. Cultures of the urine disclosed Escherichia coli and Proteus vulgaris. The double ureters on the right side were straightened, the excess removed, and both reimplanted into the base of the bladder by using a tunnel and cuff technique. Despite vigorous antibiotic therapy and general supportive measures, the infant died 1 month after operation, principally because of sepsis (blood cultures were positive). At postmortem examination severe bilateral hydronephrosis, hydroureter, and pyelonephritis were evident. An easily demonstrated obstruction at the ureterovesical junction on the left was present, but there was no apparent obstruction to the reimplanted ureters on the right. The bilaterally intra-abdominal testicles were otherwise not unusual. It is noteworthy that nephrostomy was not employed and that the patient died of sepsis which appeared to originate from the severe pyelonephritis, particularly the pyelonephritis on the side not operated upon.

CASE 4. L. K. was the 3 day old product (Fig. 11) of a fourth pregnancy of a normal mother. One sibling was normal but 2 other pregnancies had terminated in miscarriage. Urinalysis demonstrated a trace of albumin, occasional red blood cells, and 3 to 6 white blood cells per high power field in the centrifuged specimen. The blood urea nitrogen was 8 milligrams per cent. Cystography disclosed a large irregular bladder and slight reflux up the left ureter (Fig. 12). Intravenous pyelography showed prompt function but poor delineation of the architecture. On the sixth day, an exploratory cystotomy with retrograde pyelography was performed (Fig. 13). The left

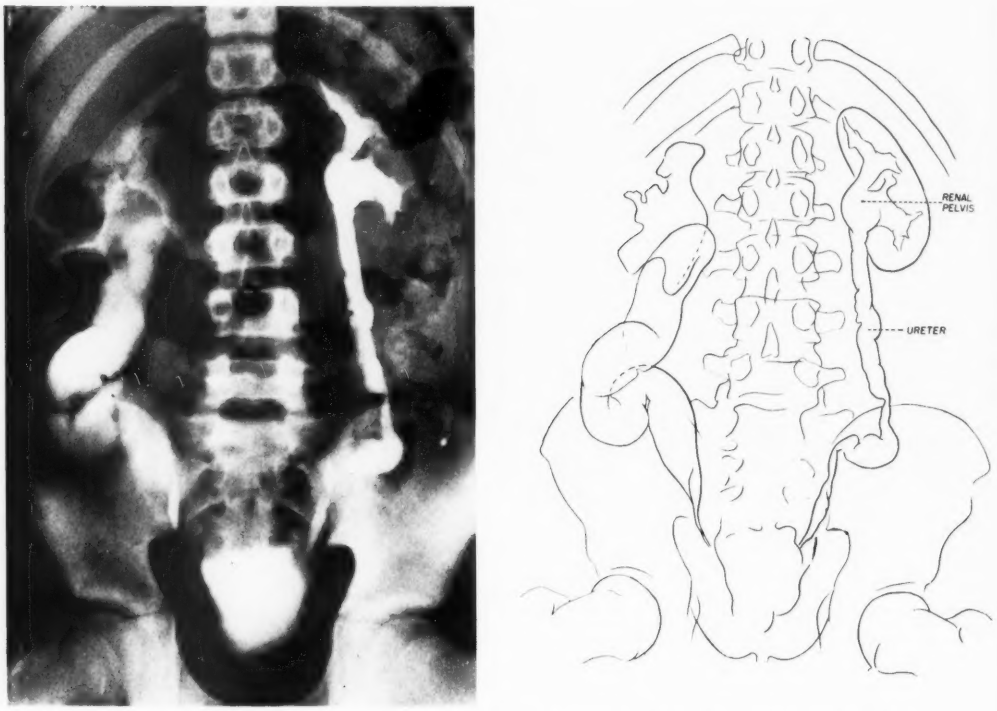

FIG. 20. Case 7. A retrograde pyelogram exhibiting a greatly dilated right ureter and a mildly dilated left ureter.

ureter was reimplanted into the base of the bladder by the tunnel and cuff technique. A right ureteral meatotomy was also performed at this time. Postoperatively the abdomen became distended, jaundice appeared, the abdominal wall became inflamed, and the child died. At postmortem examination on the fourth postoperative day, only traces of muscles could be found in the abdominal wall. The bilateral hydronephrosis and hydroureter were extreme (Fig. 14). The inflammation in the left upper urinary tract was only mild, but that in the right upper urinary tract was severe with multiple abscesses present in the renal parenchyma. The testes, grossly and histologically unremarkable for this age, were intra-abdominal. It seemed clear that the patient died largely because of the massive sepsis, and that this originated in the undrained right upper urinary tract. It is worthy of note that nephrostomy was not employed on either side.

CASE 5. J. R. was the product of the third normal pregnancy of a 26 year old mother whose 2 daughters were without abnormality. The characteristic appearance and bilateral cryptorchism were noted in the delivery room (Fig. 15), and the patient was transferred at once for urologic investigation. Urinalysis disclosed 1 to 3 red blood cells, 4 to 7 white blood cells, and an occasional coarsely granular cast per high power field in the centrifuged specimen. The blood urea nitrogen was 27 milligrams per cent. On the fourth day of life an intravenous pyelogram indicated very poor function and severely dilated ureters. Cystography via a transurethral catheter demonstrated a large bladder, bilateral ureteral reflux, dilated ureters, and delayed emptying of the ureters through the area of the ureterovesical junctions. An injection cystourethrogram disclosed a large irregular bladder (Fig. 16). Bilateral nephrostomy was carried out under local anesthesia on the fifth day of life. The renal parenchyma was estimated to be about half the normal thickness. Improvement has been slow and the child is awaiting further corrective procedures.

CASE 6. R. V. was the product of the third pregnancy of a normal mother. He had a healthy sister but the other pregnancy had terminated in miscarriage. The characteristic deformity with bilateral cryptorchism had been noticed at birth, but the necessity of a urologic investigation was apparently not realized until he entered the Columbia-Presbyterian Medical Center at the age of 15 months because of a severe upper respiratory infection. Lattimer in-

cluded this case in his recent report and graciously agreed that we also include it since the late follow-up has been under our supervision. Bilateral nephrostomy and later bilateral ureteroneocystostomy were performed. The vesical outlet was revised twice, but because of residual urine and an atonic bladder, the cystostomy had been maintained. Flaring of the lower rib cage and a pigeon breast deformity were evident. Neurologic examination revealed no abnormality. When we first saw the patient at the age of 3 years, the urine was mildly infected, the blood urea nitrogen ranged from 23 to 33 milligrams per cent, and the P.S.P. excretion via the cystostomy tube was 25 per cent in 2 hours and 45 per cent in 12 hours. Intravenous pyelography indicated diminished function with moderate bilateral hydronephrosis. Cystography demonstrated bilateral reflux (Fig. 17). Emptying of the straightened ureters was found to be excellent. Nearly 2 years later, because of painful bladder spasms and after determining that the patient could void without a residual in the bladder, the cystostomy opening was permitted to close. The urine became uninfected, but at irregular intervals the suprapubic site has drained a few drops of urine. When the patient was 10 years old, his local physician reported that the blood urea nitrogen fluctuated about 30 milligrams per cent, that voiding was adequate, and that the urine was still uninfected. The patient had been asymptomatic and attending school wearing an abdominal binder. It seems clear that this patient has progressed well because the renal damage was not too severe in the beginning and especially because of the improved drainage provided by the surgical procedures outlined.

CASE 7. While this patient was undergoing surgery at another hospital, an acutely tender mass in the lower right quadrant of the abdomen was discovered to be a tremendously dilated and tortuous ureter which collapsed during manipulation. The acute episode was thereby relieved. Intravenous pyelography then demonstrated bilateral hydronephrosis and hydroureter (Fig. 18). Cystography did not reveal ureteral reflux (Fig. 19). Cystometric studies indicated an atonic bladder with a capacity of over a thousand cubic centimeters. Retrograde pyelography demonstrated a greatly dilated right ureter, an only mildly dilated left ureter, and a surprisingly good thickness of renal parenchyma bilaterally (Fig. 20). Of some interest is the fact that the ureters were dilated almost only in the portions above the pelvic brim. We saw the patient in consultation with Dr. Dovell Bonnett. The patient was a tall, rather well developed boy, 15 years of age, with a normal penis, abundant pubic and axillary hair, and a slight moustache. The scrotum was empty but otherwise well developed. The testes could not be identified. The left rectus muscle was easily detectable and appeared to function satisfactorily, but the right one was smaller and weaker. The diffuse muscular defect appeared limited to the right side of the abdomen. The tone of the anal sphincter was considered to be somewhat lax. Observation showed that the patient was able to void and to maintain the urinary stream only so long as he strained. The characteristic appearance of the abdomen had been noted at birth, and when he was 2 years old pyuria had been found at the time of an attack of fever and dysuria. Intramuscular injections had been given at the age of 5 years in an unsuccessful attempt to produce testicular descent. Bowel function had always been satisfactory and he had been able to carry on normal activities wearing an abdominal support. Further studies and therapy have been refused.

SUMMARY AND CONCLUSION

The presence of the syndrome of congenital deficiency of abdominal musculature and obstructive uropathy can be determined at a glance. The exact embryologic cause of the complex anomaly is unknown. Prompt and accurate evaluation of the urinary tracts is essential to intelligent management. Corrective therapy usually requires urinary drainage, preferably by nephrostomy, as the first step. Plastic procedures on the ureters and vesical outlet will usually be required. Adequate prompt therapy can prevent early death and urinary invalidism in at least some cases.

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RADIATION INJURY TO THE SIGMOID AND RECTUM

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THE END RESULTS of radiation therapy for pelvic malignant tumors, particularly carcinoma of the cervix, have been extensively reported in the literature. However, relatively few reports have been made with regard to the surgical management of lesions of the small intestine, sigmoid, and rectum that may occur as a result of radiation.

Severe symptoms resulting from an acute inflammatory reaction in the bowel wall may occur within a few months after treatment. On the other hand, the first indication of the extent of radiation damage may be a sudden perforation of the small intestine, colon, or rectum a year or more later. Symptoms of obstruction may occur early or late, and they may be progressive or transitory.

We have reviewed our experiences with this problem in a series of patients who were seen at the Lahey Clinic between 1935 and 1957. Patients with minor rectal symptoms which occurred during or after radiation were not included in this study. Such minor symptoms were readily controlled by symptomatic treatment, and the patients did not require hospitalization or operation. Those patients with injuries of the small intestine not associated with proctitis or rectal strictures also were not included. In nearly all of these cases, symptoms of small intestinal obstruction developed months or years after radiation of the abdomen. The essential point to remember is that the intestinal obstruction may be caused by adhesions or cicatricial changes secondary to radiation and not necessarily by recurrence of the malignant disease.

Forty-one patients sustained serious injury to the rectum and small intestine or to the sigmoid or rectum alone as a result of radiation therapy for pelvic cancer. This group includes 22 cases of severe proctitis, 3 of sigmoiditis, 12 patients with rectal stricture, and 4 patients with sigmoid stricture. Five instances of necrosis of the small bowel and 3 fistulas between bowel and genitourinary organs were encountered in this group of 41 patients.

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INCIDENCE AND PATHOGENESIS

Since patients with mild injuries were not included in our study, we could not determine the frequency of this complication. In a study of 640 patients treated for carcinoma of the cervix, Buie and Malmgren found a 5.07 per cent incidence of complications, with 3.4 per cent of these related to the gastrointestinal tract. These patients had been treated for carcinoma of the cervix with 4,000 to 8,000 milligram hours of radium and 6,000 to 12,000 roentgens, and had had a follow-up of 6 months or more.

The seriousness of this complication is shown by Aune and White who reported 6 cases of ileitis and 17 cases of proctosigmoiditis, with 3 deaths. The deaths were caused by peritonitis secondary to perforation of a radiation ulcer; 2 of these ulcers were located in the rectosigmoid and 1 in the ileum. Requarth and Roberts reported 12 cases with 4 deaths. They found a wide variation in individual susceptibility to radiation injury. The total dose of radiation which produced the injury varied from 4,750 to 14,400 roentgens and from 50 to 8,400 milligram hours of radium. Todd reported a total incidence of 5 per cent for this complication and an appreciable number of early deaths following apparently minimal injury to the bowel. Aldridge reported intestinal injuries of varying severity in 1 of every 4 or 5 patients treated for carcinoma of the cervix. He suggested several

ways of reducing the occurrence of this serious complication.

The interval between treatment and onset of symptoms varied considerably from case to case. Aune and White found that symptoms of radiation injury to the bowel may appear from 1 month to 9 years after treatment. The pathologic changes that occur following pelvic irradiation were well outlined by Bacon in 1937. The earliest change is an acute inflammatory reaction, with edema, hyperemia, and spasm; this may subside without further complications. In the more serious cases, the primary injury to the blood vessels in the intestinal wall leads to endarteritis, thrombosis, and subsequent infarction. The mucosa then ulcerates, leaving single or multiple irregular, superficial erosions which may progress to deep, punched-out, discrete ulcers with a ragged, grayish base and sharp margins. The surrounding mucosa becomes thickened and indurated with numerous telangiectases presenting a characteristic picture on proctoscopic examination. The ulcer may then perforate into the peritoneal cavity, producing generalized peritonitis or into the vagina or bladder, producing a rectovaginal or rectovesical fistula. If the perforation takes place into the perirectal tissues, an ischiorectal abscess will develop.

Later, as the lesions heal, bands of scar tissue may constrict the intestine and produce obstruction. The primary radiation may produce a diffuse mass of fibrous tissue involving all the pelvic structures, a condition which is difficult to differentiate from the "frozen pelvis" caused by recurrent carcinoma.

The three phases of radiation reaction—edema and hyperemia, followed by ulceration, followed by stricture formation—are each associated with a variable symptom complex. These patients may be divided into two main groups: those with proctosigmoiditis manifesting itself either as colitis or obstruction, which usually appears within the first 6 months of treatment, and those in whom obstruction develops, usually as a result of injury to the small intestine, with symptoms appearing between 5 months and several years after treatment. In either group, the lesion may go on to ulceration and perforation. Craig and Buie believe that if the malignant lesion has been destroyed, the factitial lesion usually will heal, although 1 or more years may elapse before healing is complete. Fourteen of 200 patients in their series required surgical intervention.

In a detailed analysis of 77 cases, Wigby has shown a definite lack of correlation between the dosage of radiation or mode of administration and subsequent damage to the distal bowel. He noted damage to the large intestine in 57 per cent of cases in which the genital carcinoma was destroyed by radiation. He also believes that post-radiation stricture of the distal large bowel, unlike ureteral stricture, is often temporary and always amenable to surgical treatment.

SMALL BOWEL INJURY

Serious radiation injury to the small intestine may follow radiation therapy to the abdomen or pelvis. As Jones has pointed out, the symptoms are usually those of intermittent obstruction of the small intestine—weight loss, nausea, and vomiting, with crampy, intermittent abdominal pain. These symptoms are often indistinguishable from those of recurrent carcinoma involving the small intestine. For this reason, such cases are frequently considered hopeless and the patients may be denied operative treatment. In our experience, serial study frequently fails to demonstrate the lesion. Pressure upon the sigmoid may be shown on the barium enema examination, or a soft tissue mass seen in the pelvis on the roentgenogram of the abdomen. Frequently a pelvic mass which has escaped detection on vaginal examination can be felt by rectal examination. These patients deserve an exploratory laparotomy and such cases should not be dismissed as inoperable without biopsy proof of intra-abdominal or pelvic recurrence. The seriousness of allowing

TABLE I.—SIGMOIDITIS AND STRICTURE OF THE SIGMOID

Case	*Age, years*	*Radon or radium*	*X-ray*	*2 m.e.v. x-ray*	*Interval between end of treatment and onset of proctitis*	*End result*
1	49	7200 mgm. hrs. 2880 mgm. hrs. 2 series	4000 r. 2 series		6 months (2nd series)	Bowels normal; no recurrence in 10 years
2	66 M			8000 r	9 months	Bowels normal; no recurrence 9 years after original diagnosis and 2 years after 2 m.e.v.
3	59	? dose	? dose		36 months	Dead in 4 years; recurrent tumor compressing iliacs on venogram
4	55	? dose			8 months	Resection of sigmoid, end-to-end; bowels normal; no recurrence in 3 years
5	39	8000 mgm. hrs.	? dose		2 weeks	Colostomy 1950; rectal stricture developed in 1954; no recurrence in 4 years
6	50	5760 mgm. hrs.	? dose		? months	2 stage resection; bowels normal; no recurrence in 9 months
7*	46 M			8000 r	6 months	Colostomy and cystotomy; no recurrence 11 months

Diagnosis was carcinoma of the cervix, with the following exceptions: carcinoma of the cervical stump—Case 4; carcinoma of the bladder—Cases 2 and 7 (both males).
*Perforation with retrovesical abscess.

these patients to go untreated is well illustrated by the following case report.

A 60 year old woman had been given primary therapy of 9,000 roentgens by a 2 million volt x-ray unit for carcinoma of the cervix, stage 3. Seventeen months after completion of therapy, bleeding, diarrhea, vomiting, and weight loss occurred. A barium enema showed narrowing of the rectum. Proctitis was present at the 4 inch level. A mass had previously been noted on rectal examination 6 months after completion of therapy, and was still palpable at the time of the onset of symptoms. The proctitis subsided, but symptoms of partial intestinal obstruction continued for 3 years. She was admitted to the hospital 3½ years after radiation treatment and died 24 hours after admission. Autopsy revealed no residual tumor. Death was caused by generalized peritonitis secondary to radiation necrosis of the ileum with perforation.

The delayed symptoms of nausea, weight loss, and abdominal pain were not caused by radiation proctitis or by recurrence of the carcinoma. In retrospect, it seems obvious that a laparotomy should have been performed when the low grade obstructive symptoms persisted, especially when a mass was palpable in the pelvis on rectal examination. Five patients in this group died as a direct result of radiation injury to the small intestine. In 2 cases no residual malignant disease was found at autopsy. It should also be noted that only 2 of 5 patients with serious injury of the small intestine had been submitted to any previous abdominal operation. A history of previous operation leading to pelvic adhesions involving the small intestine is not essential for the production of radiation necrosis of the ileum.

White and Finn urge that these patients be kept under constant supervision, since the disease is progressive. In their series, the occurrence of perforation with abscess formation was invariably fatal.

SIGMOID AND RECTUM

Three patients had sigmoiditis, and stricture of the sigmoid was present in 4 instances (Table I). The presenting symptoms and clinical picture were similar to those seen in cases of proctitis and rectal stricture. In the patient seen most recently because of stricture of the sigmoid, perforation of the sigmoid and a retrovesical abscess developed. All 4 patients were alive 1 to 4 years later with no evidence of recurrent disease. Presumably, the interposition of a redundant sigmoid in the cul-de-sac behind the cervix led to the occurrence of the maximum injury in this segment of the intestine.

Twenty-two patients had severe proctitis

TABLE II.—PROCTITIS

Case	Age, years	Radon or radium	X-ray	2 m.e.v. x-ray	Interval between end of treatment and onset of proctitis	End result
8	60	3772 mgm. hrs.		6000 r	8 months	Bowels normal; no recurrence 30 months
9*	60			9000 r	17 months	Perforation of ileum—no operation; no tumor at autopsy (1956)
10	46	4500 mgm. hrs.	2000 r	5175 r 2 series	During 2nd series	Dead in 7½ years of recurrent tumor
11†	53	Radon	2100 r	10,000 r 2 series	8 months (2nd series)	Dead in 3½ years of recurrent tumor
12	32	6682 mc. hrs.			1 month	Wertheim hysterectomy; negative pathologic findings; no recurrence 12 years
13	47	4484 mgm. hrs.	10,000 r 2 series		5 months (2nd series)	Dead in 2 years of recurrent tumor
14	62			8000 r	10 months	Massive rectal bleeding 1956; asymptomatic 1957; no recurrence 2 years
15*	47	5700 mgm. hrs.		6000 r	5 months	Necrosis of ileum and rectosigmoid; died after operation; no tumor at autopsy (7 months)
16	40	6000 mc. hrs.	? dose		2 months	Dead in 4 years of recurrent tumor
17	60	4600 mc. hrs.	? dose		6 months	Dead in 1 year; small bowel obstruction; ? radiation fibrosis
18	59	2500 mc. hrs.	8000 r		1 month	Dead in 28 months of recurrent tumor
19	62	? dose			2 weeks	Lost to follow-up after 8 months
20	39	? dose	? dose		1 month	Bowels normal; no recurrence 18 years
21	52	? dose	? dose		36 months	Lost to follow-up after 1 month
22	58			5800 r	End of 2 m.e.v. treatment	Bowels normal; no recurrence 5 years
23	57	4800 mgm. hrs.		5800 r 2 series	During 2nd series	Dead in 12 months; cause of death obscure; ? recurrence
24	58			6000 r; 3000 r 2 series	End of 2nd series	Dead in 3 years of recurrent tumor
25‡	50	3900 mgm. hrs.		6000 r	9 months	Resection of uterus and fistula; bowels normal; no recurrence 36 months
26	52	3000 mgm. hrs.		6000 r	End of 2 m.e.v. treatment	Dead in 3 years; pulmonary metastases
27	50		2400 r 6250 r 3 series	8000 r 2 series	1 month (2nd series)	Dead in 4 years of recurrent tumor
28*	58		9500 r	5900 r 2 series	During 2nd series	Dead in 5 years; small bowel obstruction; cause of death uncertain
29	37	? dose	? dose		5 months	Bowels normal; no recurrence 35 months

Diagnosis was carcinoma of the cervix, with the following exceptions: carcinoma of the cervical stump—Cases 8, 21, and 26; carcinoma of the ovary—Case 27.
*Necrosis of the ileum.
†Rectovaginal and vesicovaginal fistulas.
‡Enterouterine fistula.

(Table II). Four of these patients were subjected to palliative operation—4 colostomies and 1 resection of the small bowel. One of the patients undergoing palliative colostomy subsequently required abdominoperineal resection for control of massive rectal hemorrhage resulting from intractable proctitis with ulceration.

Rectal strictures were present in 12 cases (Table III). The presenting symptoms were those of severe proctitis with progression to partial or complete obstruction of the distal colon. Five of the 7 surviving patients were submitted to operation, and both of the patients who died of recurrent disease had undergone palliative colostomy.

The time of onset of the symptoms was not related to the elimination of the pelvic cancer by radiation. The average duration between the first treatment and the onset of symptoms of proctitis was 4 months in the surviving group and 2.4 months in those who died of recurrent disease. The difference may be accounted for in part by the fact that secondary supervoltage therapy was more widely used in the latter group. Significant intestinal damage was evidenced by persistent symptoms usually occurring

TABLE III.—STRICTURE OF THE RECTUM

Case	*Age, years*	*Radon or radium*	*X-ray*	*2 m.e.v. x-ray*	*Interval between end of treatment and onset of proctitis*	*End result*
30*	53	? dose	? dose	5700 r 2 series	During 2nd series	Dead in 2 years, recurrent tumor
31†	36	6000 mgm. hrs.	3500 r	6000 r 2 series	3½ months (2nd series)	Colostomy 1952; resection of ileum 1953; no recurrence 7 years
32	49	? dose			2 weeks	Colostomy 1949; resection of sigmoid 1949; closure of colostomy 1952
33†	59		4000 r	8000 r 2 series	6 months (2nd series)	Resection of ileum 1956; question of vaginal recurrence 6 years
34	42	4500 mgm. hrs.	2520 r		2 weeks	Slight stricture; no treatment; no recurrence 4 years
35	49	6000 mgm. hrs.	7200 r		3 months	Bowels normal; no recurrence 12 months
36	34	? dose	? dose 1500 r 2 series		? months	Dead in 4 years of recurrent tumor
37	40	? dose	? dose		? months	Dead in 7 years; congestive heart failure 4 years after loop colostomy for stricture
38	52	3012 mc. hrs. 1500 mgm. hrs.		6043 r 2 series	30 months (2nd series)	Dead of pulmonary embolism after colostomy; recurrence 6 years; no tumor 7 years
39	53	? dose	? dose		6 months	No follow-up
40	40	? dose	? dose		? months	3 stage resection; bowels normal; no recurrence 36 months
41	54	? dose	? dose		? months	Mild symptoms from stricture; no recurrence 6 years

Diagnosis was carcinoma of the cervix, with the following exceptions: fibroid uterus—Case 32; endometrial carcinoma—Case 33; carcinoma of the cervical stump—Case 41.
*Rectovesical fistula.
†Necrosis of ileum.

toward the end of therapy or shortly thereafter. In patients receiving a secondary course of radiation the symptoms could occur at any time. The onset of proctitis was evidenced by the occurrence of diarrhea, rectal bleeding, and pain. In some cases the diarrhea may be severe and lead to symptoms of electrolyte imbalance such as a notable decrease in serum potassium. The bleeding may be so severe as to require abdominoperineal resection.

From our experience, the following plan of therapy was evolved. If symptoms are not completely controlled within 2 weeks after onset, the patient should be hospitalized. It is essential that an adequate proctosigmoidoscopic and pelvic examination be carried out, using anesthesia if pain prevents an adequate examination. A barium enema study is made as soon as the rectal discomfort has subsided sufficiently to permit it.

A bowel management program is instituted immediately after the initial examination. This consists of a bland, low residue diet, sedation, antispasmodics, intestinal antibiotics, hydrocortisone enemas, bed rest, and general supportive measures. Patients with severe bowel injuries resulting from radiation therapy should be treated in the hospital. Three patients admitted with what appeared to be a rectal stricture were relieved of symptoms after 10 days of hospital treatment and 2 recovered completely. In several instances, complete rectosigmoidal obstruction (as indicated by barium enema examination) subsided completely on the therapeutic program outlined. Subsequent studies after barium enema revealed no abnormality. In our experience, stricture formation is not an inevitable sequela of severe proctitis. This may be the type of patient in whom a cure has been reported following repeated rectal dilatations.

Some patients with severe proctitis or early stricture will not be relieved by these measures. If no significant improvement occurs after 2 or 3 weeks of treatment in the

hospital, a proximal colostomy should be established. This measure should also be seriously considered if a significant amount of bleeding occurs and persists, or if symptoms recur following conservative treatment in the hospital. The following case report well illustrates several of the problems associated with severe radiation injury to the rectum.

A 40 year old mother of 3 children had had a diagnosis of stage 1 carcinoma of the cervix in November 1954. She was given x-ray and radium treatment at that time and was apparently well until December 1955, at which time acute abdominal symptoms developed in a period of 24 hours. An exploratory laparotomy was performed and a large perforation of the rectosigmoid encountered. Induration and thickening were noted in the proximal portion of the bowel, indicating the presence of chronic, partial obstruction. The perforation was closed by using the fundus of the uterus, the left tube, and a free omental graft. A transverse loop colostomy was made through a separate incision. The patient recovered.

The patient was first seen at the Lahey Clinic in August 1957. Pelvic examination revealed that the cervix was small and fixed and the vaginal mucous membrane was normal. A firm mass was palpable posterior to the cervix. On rectal examination a complete stricture could be felt; this would not admit the tip of the finger. Proctoscopic examination showed telangiectases and stenosis at the 3 inch level. Bleeding did not occur. An intravenous pyelogram revealed slight dilation of the right renal pelvis and calyces with moderate dilation and tortuosity of the ureter. Blood count, urinalysis, sedimentation rate, and nonprotein nitrogen were within normal range. Operation was performed on October 2, 1957 after inserting a No. 7 ureteral catheter into each ureter. The sigmoid and rectum were mobilized by sharp dissection down to the levator muscles. The rectum was divided 2 inches from the anus; 6 inches of indurated, contracted sigmoid were resected and an end-to-end anastomosis was made. Two drains were placed in the pelvis. The patient did well postoperatively and the proximal colostomy was closed on the seventh postoperative day.

Examination of the pathologic specimen showed an area of stricture 2 millimeters in diameter in the midportion of the resected specimen of rectosigmoid. The mucosa had been destroyed and was replaced by smooth, grayish tissue with 2 areas of ulceration adjacent to the stricture. The wall of the colon was 7 millimeters thick above the stricture. On microscopic examination, colitis with ulceration of the mucosa and hypertrophy of the muscularis was noted. No tumor was found in any of the removed tissues. The patient's convalescence was uneventful and she has remained well. Bowel function is normal.

In this case, the first indication of serious damage to the rectal wall was the sudden perforation 13 months after treatment. The patient survived the generalized peritonitis only because prompt surgical intervention and intensive supportive therapy were instituted. Since no evidence of recurrent tumor could be found almost 3 years after treatment of the carcinoma of the cervix, an attempt to restore intestinal continuity was justified.

Because of the severity of the radiation injury it was necessary to resect the involved rectum. The small caliber of the sigmoid and rectum made subsequent stenosis at the suture line a serious hazard. It was thought that the risk of obstruction was greater than the risk of leakage, and for this reason the proximal colostomy was closed on the seventh postoperative day.

SUMMARY AND CONCLUSIONS

A review of 41 patients with serious injury to the small bowel and sigmoid or rectum following pelvic radiation has been presented. With the increasing use of radiation, surgeons may anticipate the necessity of dealing with this type of injury more frequently in the future. Hospitalization and intensive conservative treatment of patients with severe proctitis may provide relief and eliminate the necessity for operation. If conservative treatment fails, a temporary colostomy may be sufficient to permit the acute process in the rectum or sigmoid to subside. Symptoms of obstruction of the small intestine may result from adhesions or stricture of the ileum secondary to radiation treatment of a pelvic malignant tumor. Sudden perforation of the ileum, sigmoid, or rectum may occur months or years following treatment. The abrupt onset of peritonitis in the case of any patient who has received radiation therapy to the pelvis should be promptly investigated by laparotomy.

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POSTOPERATIVE IRRADIATION OF 86 CASES OF CARCINOMA OF THE CERVIX

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THE GRAHAMS STATED that "cancer found too deeply seated or widespread for removal at operation is rarely controlled by subsequent radiotherapy." Kottmeir and Meigs reported exceptions to these conclusions, but also agreed that inoperable metastases in the pelvic nodes were no more curable by radiation than by surgery. These authors reported occasional control of massive metastases, concluding that, at times, radiotherapy can be effective. Brunschwig and Daniel reported that if disease was left behind following pelvic exenteration and if no irradiation was administered, no survivals resulted. In their series of 36 patients who underwent exenteration and in whom there was residual disease, the average survival was slightly over 3 months. One patient lived 16 months.

In this article an attempt will be made to answer the question as to whether or not postoperative irradiation is of value. Four postoperative categories have been defined and will be presented with their respective end results.

MATERIAL AND METHOD

Since 1947 the role of surgery as the primary treatment for cancer of the cervix has been under study at Memorial Hospital. The vast majority of the patients so treated did not receive postoperative x-ray therapy. The 86 cases reported in this article comprise all the patients referred for postoperative x-ray therapy by the gynecology service to the Department of Radiation Therapy during the period 1948 through 1956. None of the 86 patients had received preoperative irradiation.

All stages of carcinoma of the cervix were surgically treated by the gynecology service. The decision to treat all stages of carcinoma of the cervix surgically required a wide variety of procedures ranging from exploratory operations without tumor excision to various radical curative operations, each appropriate for the degree of cancer involvement. In view of this fact, we were confronted with a wide variety of postoperative conditions. Our material was therefore divided into the following categories according to the postoperative findings:

Category I—The completely excised group, 15 cases. In this category the primary disease and regional nodes had been completely excised. This fact was established by the absence of gross disease in the pelvis, either primary or metastatic nodes, and by pathologic evidence that margins of excision showed no tumor cells.

Category II—The postoperative recurrent cancer group, 27 cases. This group had had no evidence of residual disease grossly or histologically at the completion of surgery, but cancer had recurred in the follow-up period.

Category III—The postoperative persistent cancer group, 24 cases. These patients had had persistent cancer at the completion of the operation.

A. This category was subdivided into 11 cases of proved persistent cancer; by definition, these patients had cancer left behind in the pelvis or nodes, proved by biopsy. In other cases there was histologic evidence of the presence of cancer found in the margins of excision.

B. Thirteen other cases were interpreted as presumed persistent cancer when the surgeon believed that cancer remained, or the pathologist stated that the cancer cells were seen near the margins of the excision.

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TABLE I.—MAIN DATA ON COMPLETE SERIES

	Category					
	I	*II*	*III*		*IV*	
			A	*B*		*Total*
No. of cases	15	27	11	13	20	86
L. of N. stage I and II	15	14	11	13	4	57
III and IV	0	6	0	0	10	16
Unstaged	0	7	0	0	6	13
Negative nodes	8	13	4	0	0	25
Highest level pos. nodes						
Parametrial	0	3	1	0	0	4
Obturator	4	2	1	1	0	8
Hypogastric	0	3	0	1	0	4
Ext. iliac	0	1	1	3	0	5
Common iliac	2	3	2	2	8	17
Para-aortic	2	0	1	0	12	15
Distant	0	0	0	0	8	8
Surgical procedures						
Hyst. and node exc.	10	13	4	7	0	34
Cerv. stump and node	2	3	0	1	0	6
Exenteration						15
Anterior	1	1	0	2	0	
Posterior	0	1	1	1	0	
Total	0	5	3	0	0	
Schauta	2	0	0	1	0	3
Exploration						20
Others	0	3	3	2	0	8
Previous therapy elsewhere					15	
No previous therapy						52
No further surg. prior to x-ray						73

Category IV—The explored group, 20 cases. In these cases excision was technically impossible because of the extent of the pelvic disease or because of the fact that extrapelvic or distant nodes contained cancer, even though the primary disease may have been resectable.

Within categories II and IV patients were treated even in the face of what appeared to be hopelessly extensive disease. Even distant metastases did not contraindicate treatment. These areas of distant spread were treated simultaneously with the pelvic disease. When curative radical doses could not be administered, palliation was attempted.

The clinical characteristics of the total series of carcinoma of the cervix cases herein reported in no way differed from the generally known statistics concerning age, race, or gravidity. Patients in the fourth through fifth decades predominated. Only 1 patient was under 30 years of age and 1 was over 70 years of age. Fifty-two patients had had no treatment prior to surgery at Memorial Center. Eighteen patients had had irradiation for cancer of the cervix and 16 others had had surgical procedures elsewhere prior to operation at Memorial Center.

TABLE II.—LEAGUE OF NATIONS STAGE AND HISTOLOGIC GRADE

	Grade					
Stage	*Unstated*	*1*	*2*	*3*	*4*	*Total*
Unstated	4	0	4	5	0	13
I	6	0	12	6	0	24
II	1	0	13	19	0	33
III	3	0	3	3	1	10
IV	1	0	2	3	0	6
Total	15	0	34	36	1	86

TABLE III.—LEAGUE OF NATIONS STAGE AND SURGICAL PROCEDURE

Stage	*Hyst. and node dissect*	*Excision cervix and node*	*Exenter.*	*Exploration*	*Others*	*Total*
Unstated	2	0	3	8	0	13
I	12	4	1	1	6	24
II	19	2	4	3	5	33
III	1	0	4	5	0	10
IV	0	0	3	3	0	6
Total	34	6	15	20	11	86

*Others include Schauta.

TABLE IV.—TREATMENT CATEGORIES ACCORDING TO POSTOPERATIVE FINDINGS

	Category					
	I	*II*	*III*		*IV*	*Total*
Surgical procedure			*A*	*B*		
Hyst. and node	10	13	4	7		34
Cerv. stump & node	2	3	0	1		6
Exenteration						
Total	0	5	3	0		8
Ant.	1	1	0	2		4
Post.	0	1	1	1		3
Others						
Wertheim, Cerv. excision, Schauta	2	4	3	2		11
Exploratory laparotomy					20	20
Totals	15	27	11	13	20	86

Table I is a composite table containing the main characteristics of the total series of 86 patients and the identifying features of each of the 4 x-ray treatment categories previously defined. Note again the large number (52) who had no previous treatment, as well as the majority of patients (73) whose condition did not require or permit a second surgical procedure before the onset of x-ray therapy. Also note, that of the 4 treatment categories, the explored group, category IV, had the largest number of patients previously treated before coming to Memorial Center. Furthermore, such features as League of Nations staging, the frequency of negative regional nodes, the number of cases of positive para-aortic nodes, and finally, the proportion of radical

hysterectomies to exenteration procedures serve to distinguish one category from the other.

Table II gives the League of Nations stage and histologic grade for all patients. When grade was stated, all except 1 case were graded as 2 or 3. Correlation between grade and stage of disease was investigated, but as shown in this table no significant differences were found.

Table III related League of Nations stage to the surgical procedure performed. As anticipated, favorable staging was indication for radical hysterectomy and node dissection, whereas more advanced stages were treated by more extensive procedures or by exploration only.

Figure 1 shows graphically the information presented in Table I in respect to the highest level of positive nodal metastases. Distant nodes refer to nodes beyond the para-aortics, most usually inguinal or supraclavicular. It is not possible to present the total number of positive nodes in each case nor the degree of involvement in each positive node since this information is not available.

For each operative procedure, indications for postoperative x-ray therapy varied depending upon in which of the four postoperative treatment categories the case was placed. This is shown in Table IV. Note that 14 of the 15 exenterations referred had either histologic or clinical evidence of disease at the time of x-ray therapy. Since advanced League of Nations staging is common in this group, evidence of disease at the time of x-ray therapy was expected. However, even among the favorably staged cases in patients who underwent radical hysterectomy or cervical sump excision, with node dissection, there was a high proportion with histologically proved disease at the onset of x-ray therapy. However, conclusions as to the over-all surgical results cannot be drawn from our series since, in general, referral of postoperative cases for x-ray therapy indicated a high probability that as a group they represented surgical failures.

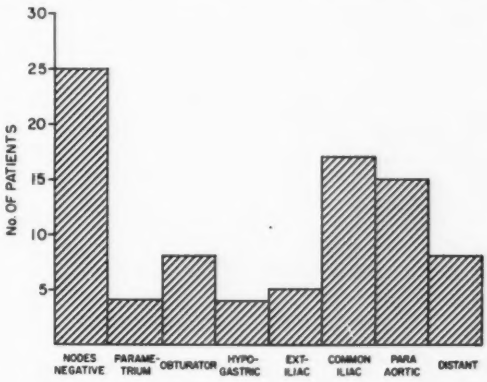

FIG. 1. Graph showing level of nodal metastases in series of 86 cases of cancer of cervix.

Whenever possible, histologic proof was obtained to establish the presence of disease. In postsurgical recurrent cancers, a clinical mass increasing in size, even though the location did not permit biopsy, was considered sufficient reason to justify x-ray therapy.

The technical factors of irradiation are summarized in Table V. The majority of patients were treated with one million volt x-rays. Parallel opposing pelvic or abdomi-

TABLE V.—FACTORS OF IRRADIATION

	No. of cases	
Kv.		
1 m.e.v.	71	
Co^{60}	2	
250 kv.	12	
Others	1	
		86
Field		
Pelvic	53	
Abdom.-pelvic (inverted T)	13	
Abdom.-pelvic	4	
Others	16	
		86
Field size		
Small (100–200 sq. cm.)	21	
Medium (200–400 sq. cm.)	51	
Large (400 sq. cm.)	14	
		86
Tissue dose		
Less than 3,000 r	17	
3–5,000 r	65	
5,000 r	4	
		86
Days treatment		
More than 21	12	
21–42	60	
Greater than 42	14	
		86

TABLE VI.—FEATURES OF 11 SURVIVORS WITH NO EVIDENT DISEASE FOLLOWING POSTOPERATIVE X-RAY THERAPY (1948 TO 1955)

Category	*Patient*	*L. of N. stage*	*Histologic grade*	*Pathology*	*Surgical procedure*	*Highest node level*	*Months post-op. to x-ray*	*Location of recurrence*	*Indications for x-ray therapy*	*Modality*	*Tumor dose, r*	*Months survived post. x-ray*
I	C.D.	I	3	Epid. stump	Excis. cerv. stump and nodes	Bifurcation aorta	1	—	"Prophylactic"	1 m.e.v.	4,000	62
	R.M.	I	2	Epid.	Schauta hyst.	Parametrial (negative)	1	—	"Prophylactic"	1 m.e.v.	4,000	84
	S.W.	II	2	Epid. stump	Anterior exenteration	Common iliac	2	—	"Prophylactic"	1 m.e.v.	4,200	36
	A.I.	II	3	Epid.	Hysterectomy and nodes	All negative	2	—	"Prophylactic"	1 m.e.v.	4,000	44
II	B.M.	I	2	Epid.	Total abd. hyst.	All negative	35	Vaginal vault	Recurrence	Radium	4,300	72
	A.M.	I	3	Epid.	Excis. cerv. stump and node	Left hypogastric	2	Vaginal vault	Recurrence	1 m.e.v.	3,600	32
	C.C.	II	3	Epid.	Schauta hyst.	Left parametrial	39	Exten. left lat. wall	Recurrence	1 m.e.v.	5,000	72
	B.K.	II	—	Epid.	Total hyst., vaginect., rectosig. and nodes	External iliac	2	L.L.Q. mass	Recurrence	1 m.e.v.	4,000 3,200	50
IIIB	E.J.*	—	—	Epid.	1. Prev. total hyst. 2. Vaginectomy and nodes	Bilateral obturator	1	—	Vein invasion Surgical specimen	1 m.e.v.	4,000	46
	E.B.	I	—	Epid.	Rad. hyst. and node	Right obturator	5	—	Invasion rt. obt. fossa	1 m.e.v.	3,000	79
	E.O.	I	2	Epid.	Excis. cerv. stump and node	Left obturator	1	—	Narrow margin excision surg. specimen	250 kv	3,500 2,500 I.V. cone	62

*Vault recurrence and invasion L-5, June, 1957. Alive with disease 56 months.

nopelvic (inverted T) fields were mainly used. In most patients a tissue dose of 1,000 roentgens weekly was administered. This dose rate was modified if the systemic reactions of the patient required it. Most patients received tumor doses of between 4,000 and 4,500 roentgens. Doses of 5,000 roentgens were administered to only 4 patients. Most fields used were medium sized. A smaller number of patients were treated through larger fields. Despite the relatively large fields needed to encompass the disease and despite the dose levels delivered, the majority of patients did not experience unusual reactions during treatment nor did they develop serious late sequelae during the follow-up period.

RESULTS

Category I. Prophylactic x-ray therapy in cancerocidal doses was given whenever possible. There were 15 patients in this category. All of these patients were staged initially as League of Nations I or II. Nodes were negative in 8 cases; while in 7 others, nodes were positive, in 2 the nodes at the bifurcation of the aorta being involved, in which cases the nodes at the bifurcation (para-aortic) were excised. Ten patients underwent radical hysterectomy and node dissection, 2 had cervical stump excision and node dissection, 1 anterior exenteration, and 2 a Schauta hysterectomy. Figure 2A gives the survival times from the onset of irradiation for category I. Eight patients

have survived more than 18 months. Four of these 8 patients were still alive and free of cancer 21, 44, 62, and 77 months respectively at the time that this report was prepared.

Table VI shows the characteristics of the 4 survivors. Patient C. D., who survived 5 years, had positive para-aortic nodes at the bifurcation of the aorta although she was staged as League of Nations I.

Category II. In this group of 27 cases, as well as the entire series, treatment was completed at least 21 months prior to the time of this report. Fourteen patients in this category were staged as League of Nations I or II and 6 as stage III or IV cancer. Radical hysterectomy and node dissection were performed in 13 cases. Three cervical stump cancers and nodes were excised. In 7 other patients exenterations were done, 5 of these being total. Negative nodes were reported in 13 of the 27 operative specimens. In none of the 11 other patients with positive nodes were the para-aortic nodes involved. Twenty-one patients manifested recurrent disease within 24 months. Half of these actually recurred within 9 months of operation. In 6 cases recurrences appeared after a 2 year interval of tumor control. Recurrent disease was confirmed by biopsy in 13 cases. In 14 cases no histologic confirmation was obtained. The diagnosis in these cases was based on the presence of clinically detectable disease.

The location of these recurrences is given in Table VII. Since 1950 it has been the policy of the gynecology service to excise limited midline recurrences and refer for irradiation all unfavorable extensive recurrences. Of 27 patients, 25 had extensive unresectable recurrent cancers. Figure 2B shows the months of survival after x-ray therapy for all patients in category II. Nine patients survived 18 months or more. Four of these 9 patients are still alive at the time of this report. Table VI gives the clinical features of these 4 patients.

Category III. In many of the 24 cases in this group, there was no histologic proof of

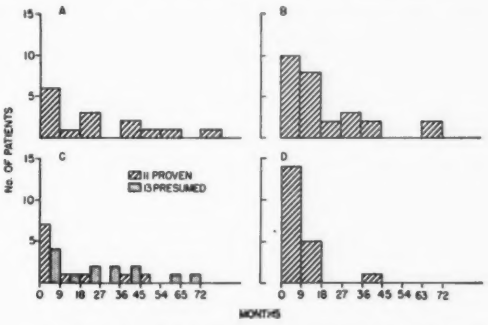

FIG. 2. Survival in months from onset of irradiation: A, in 15 cases in category I; B, in 27 cases in category II; C, in 24 cases in category III; D, in 20 cases in category IV.

persistence. Therefore, lacking histologic evidence of persistence, they have been classified as a subgroup, the presumed persistent group, category IIIB. This classification was considered necessary, since the surgeon is frequently convinced that excision was not complete. In other instances histologic evidence of cancer was found near the margins of excision. In many of these cases cancer is clinically detectable in the pelvis soon after surgery. For this reason, these patients have been considered a part of a valid subdivision of the major postoperative persistent cancer group.

Those 11 cases with histologic proof of disease persisting at the close of surgery make up the balance of this treatment cate-

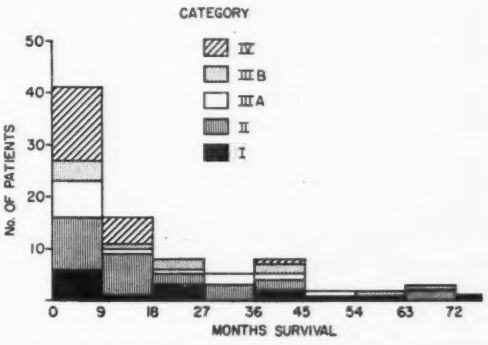

FIG. 3. Histogram showing months of survival after irradiation for each category.

TABLE VII.—LOCATION OF RECURRENCE IN 27 CASES IN CATEGORY II

Site of recurrence	*No. of cases*	*Average survival, months*
Central (midline)		
Vault	2	69
Vault, extension to bladder, rectum	4	15
Peripheral (pelvic wall)	7	10
Central and peripheral	12	7
Metastatic distant	2	7
Total	27	

gory, and we have designated them as proved persistent cancers, category IIIA.

The cases in category IIIB have the following characteristics. All in this subdivision were staged as League of Nations I or II. The operative procedures consisted of 7 radical hysterectomies and node dissections and 3 exenterations, 2 anterior and 1 posterior. One cervical stump cancer with regional nodes was excised. One patient had a Schauta hysterectomy. Although all patients in category IIIB had positive nodes at some level, none had metastatic para-aortic nodes. Figure 2C shows the months of survival after x-ray therapy for the subdivisions A and B of category III cancers. Eight patients with presumed persistent cancer survived beyond 18 months. Three of the total of 13 patients in this subdivision are alive at present without evidence of cancer. Two of the 3 long term survivors are 5 year survivors and the third is alive and well after a period of 46 months. Table VI gives the clinical features of these 3 patients.

Eleven patients had proved persistent category IIIA cancer which was proved either by biopsy of residual pelvic wall cancer, or by histologic evidence that the margins of excision had gone through cancer. All cases in this subdivision were staged as League of Nations I or II. Seven of 11 patients had metastatic nodal cancer and 1 patient had positive para-aortic nodes which were excised as part of the radical excision.

TABLE VIII.—FINAL STATUS

	No. of patients
Living without cancer	11
Living with cancer	1
Living, cancer status (undet.)	1
Dead, result of cancer	58
Dead, result of other causes	8*
Dead, result x-ray therapy complication	1†
Lost to follow-up	6
Total	86

*1 without cancer; 2 cancer status unknown.
†Questionable.

Exenteration operations were performed in 4 cases, 3 of these were total and 1 posterior. Among the proved persistent cases, 3 patients survived beyond 18 months. However, none of these 11 patients with proved persistent cancer treated with x-ray lived beyond the time intervals shown in Figure 2C.

Category IV. Figure 2D is a histogram of months of survival after x-ray therapy. Only 1 of 20 patients in category IV survived beyond 18 months. All patients in this category, including the 3 year survivor, have died.

The end results for all patients, irrespective of therapeutic indications for x-ray therapy, are summarized in Table VIII. Eleven patients were alive without evidence of cancer at the time of this report for intervals varying between 21 and 77 months (Tables VI and VIII).

Figure 3 shows not only the months of survival after x-ray therapy for all patients but also treatment categories of the survivors in each survival interval. The histogram facilitates ready comparison of survival within each interval and within each group.

Restating the results in general terms, there were more survivors living beyond 18 months in the categories I and IIIB than in categories II and IIIA. Although the postirradiation surival in category IV was unsatisfactory, a few patients did survive beyond 9 months, even in the presence of massive unresectable disease or para-aortic metastatic nodes.

The incidence of complications following x-ray treatment for the entire series of 86 patients was low. There were 6 patients who had early complications, consisting of: skin necrosis in 1, prolonged diarrhea in 4, and small bowel fistula in 1. The patients with diarrhea responded to conservative

management. Skin necrosis occurred in a patient who received a skin dose of 4,300 roentgens in 35 days on 1 million volt therapy, through a medium sized field, in a dose time normally tolerated. Skin grafting corrected this complication. The true incidence of late complications cannot be estimated since the number of long term survivors is small.

DISCUSSION

Although it was not the original intent of this study to investigate optimal tumor doses for carcinoma of the cervix, we attempted to correlate the dose administered with the final results. Table IX suggests that a dividing line at 3,000 roentgens may exist, below which patients cannot be salvaged. These patients frequently received less treatment because of poor general status or massive disease, either of which required a palliative approach.

When attempting to evaluate optimal tumor dose in relation to survival without cancer, 7 of these 11 patients could not be included in the evaluation, since they had no evidence of disease at the time x-ray therapy was administered. In 4 of these 7 patients the disease was completely excised and in 3 others there was only presumed persistent disease. Since only 4 of 11 patients now alive without evidence of cancer had proved recurrent or persistent disease at the onset of x-ray therapy, the numbers are too insignificant to allow an estimation of optimal dose.

A total of 6 (6.9 per cent) patients survived 5 years or more. Two of these patients were in category I, 2 in category II, and 2 in category IIIB. No patient in category IV survived 5 years.

Fifty-eight patients had disease proved clinically or by biopsy at the onset of x-ray therapy (20 explored, 11 proved persistent, and 27 postoperative recurrent). Two of these 58 patients survived 5 years.

We considered survival beyond 18 months good palliation; 29 patients did survive more than 18 months. Eight of these had

TABLE IX.—TUMOR DOSE AND FINAL STATUS

Tumor dose, r	*Total*	*Lost to follow-up*	*Dead of ca.*	*Living without ca.*	*Living with ca.*	*Dead, other causes*
Less than 3,000....	15	0	10	0	0	1
3,000-4,000.	24	3	14	3	1	3
4,000-5,000.	43	3	32	6	0	4
5,000.....	4	0	2	2	0	0
Total.....	86	6	58	11	1	8

*2 patients included in total only.

disease which was proved clinically or by biopsy at the onset of x-ray therapy (4 in category II, 3 in category IIIA, 1 in category IV).

Therefore, of the 58 patients with disease proved clinically or by biopsy at the onset of x-ray therapy, 8 (14 per cent) survived more than 18 months; 2 (3.4 per cent) lived 5 years.

CONCLUSION

This study indicates that postoperative irradiation administered in the presence of proved disease can bring about 5 year arrests and considerable palliation and prolongation of life to an otherwise incurable group of patients in whom further surgical efforts are of no value.

SUMMARY

Eighty-six cases of cancer of the cervix treated by surgery and postoperative x-ray were studied. This series was subdivided on the basis of the postoperative findings. Better survival and palliation were evident in those categories in which there was no demonstrable residual disease at the completion of surgery. All patients who underwent exploration in whom cancer was not excised have died.

The three categories of patients that have had better results yielding a few survivors alive and free of cancer at the time that this report was prepared are as follows: 4 patients with no known residual postoperative cancer (category I); 3 patients with presumed persistent cancer (category IIIB); 4 patients with postoperative recurrent cancer (category II).

Twenty-nine (34 per cent) patients, irre-

spective of x-ray treatment category, survived more than 18 months and experienced worthwhile palliation from irradiation. In the remainder of patients the extent of the disease in the pelvis or the presence of paraaortic nodal metastases projected radiation therapy into the unenviable position of a last resort measure.

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ARTERIAL BYPASS BELOW THE KNEE

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THE GOAL of operative treatment of segmental occlusive disease of the femoral artery is to restore pulsatile blood flow in the lower leg. In general, use of the bypass principle yields more consistently gratifying results than resection and grafting or thromboendarterectomy. Pedal pulses were restored in more than 86 per cent of the 317 patients whom we treated by the bypass graft technique for occlusive disease of the femoral artery (1). In most patients, the proximal popliteal artery is suitable for distal bypass anastomosis. Occasionally, however, a satisfactory peripheral arterial bed may be evident by arteriography, but extensive arteriosclerotic changes with narrowing or thrombosis in the popliteal artery may preclude use of its proximal portion and require concomitant exposure of the common femoral and distal popliteal arteries. Similarly combined approach to the common femoral artery and the distal popliteal or posterior tibial artery is sometimes necessary in the treatment of sudden occlusions of the popliteal artery or popliteal aneurysms as indicated by Roberts and Davis. Coexisting occlusive disease of the superficial femoral artery or proximal propagation of thrombi from such occlusions or aneurysms usually requires bypass from the common femoral to the distal popliteal or posterior tibial artery for restoration of pedal pulses. Furthermore, under any of these circumstances, aortoiliac occlusive disease or aneurysm may also be present. Effective exposure of the infragenual portion of the popliteal artery is difficult through a medial thigh incision. The awkwardness of combined abdominal, femoral, and posterior knee incisions is obvious.

The problem of combined exposure of the aortoiliac, femoral, and distal popliteal or posterior tibial arteries may be resolved by use of an anteromedial rather than posterior distal incision. Fortunately, the anatomic arrangement of the upper leg facilitates access to the distal popliteal and posterior tibial arteries through an anteromedial incision. Such an approach is surgically ideal and anatomically sound; division or splitting of muscles or tendons is not necessary and there is little or no trauma to the collateral arteries around the knee. Accordingly, this report is concerned with certain anatomic and technical aspects of this approach and its clinical application as derived from our experience.

TECHNIQUE

With the knee moderately flexed, a vertical incision is made just behind the posteromedial surface of the tibia (Fig. 1a). The crural fascia is incised vertically in the line of its fibers and its attachments to the distal inferior aspect of the semitendinosus and gracilis tendons separated to mobilize these structures superiorly (Fig. 1b and c). Retraction of the medial head of the gastrocnemius muscle posteriorly enables entrance into a fascial space in the apex of which are located the distal popliteal vessels and the tibial nerve as they cross the popliteus (Fig. 1d). This portion of the popliteal artery lies distal to the inferior genicular arteries and usually no significant collaterals arise from either this segment or the posterior tibial artery between the anterior tibial and

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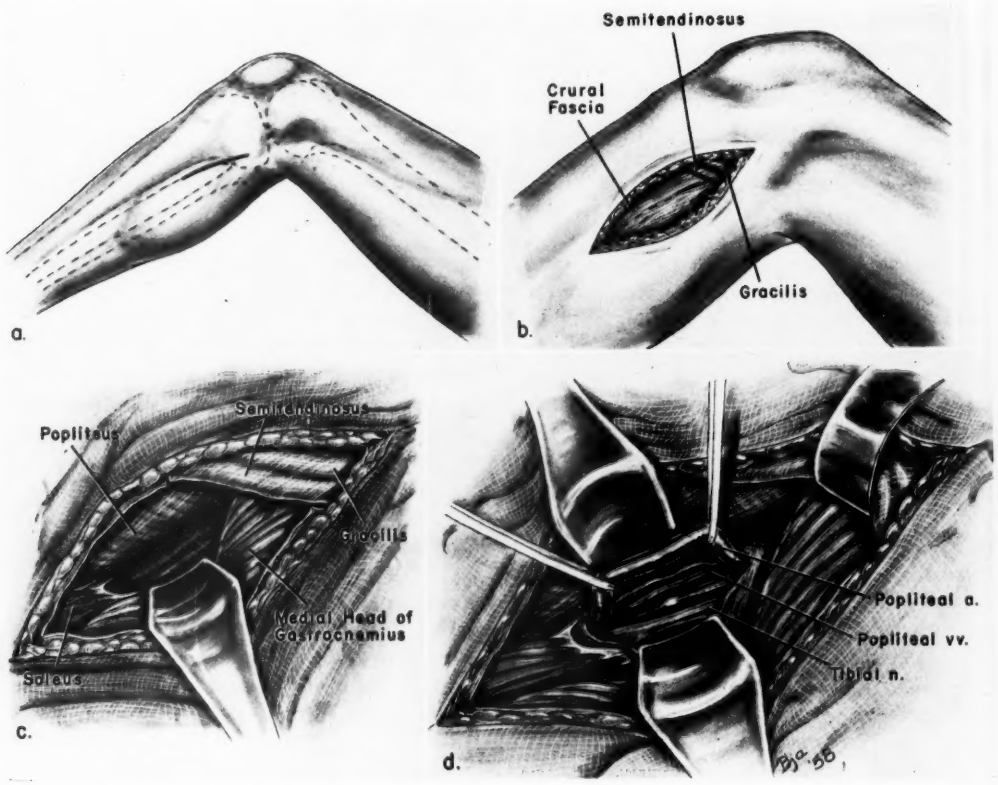

FIG. 1. Drawings showing anteromedial approach to popliteal artery below knee. a, Incision parallels medial surface of upper tibia. b, Crural fascia is divided distal to semitendinosus tendon and continued inferiorly in line of fascial fibers. Care should be exercised to avoid injury to saphenous nerve which parallels incision superficially. c, Separation of fascial attachments to inferior aspect of semitendinosus and gracilis tendons allows mobilization of these structures superiorly. Fascial space thus exposed is bounded by popliteus muscle anteriorly, soleus inferiorly, and medial head of gastrocnemius posteriorly. d, Retraction of gastrocnemius exposes popliteal artery, popliteal veins, and tibial nerve.

peroneal arteries. Because of the paucity of small branches, the artery can be mobilized and brought superficially with good exposure for distal graft anastomosis (Fig. 2). Though slightly smaller than the proximal popliteal, the infragenual segment is of sufficient caliber for satisfactory graft attachment. Of particular significance has been the finding that this segment tends to be better preserved, presumably because it lies distal to the knee joint and has not been exposed to the chronic trauma of bending.

Certain technical considerations in extension of the bypass operation below the knee would seem worthy of emphasis. In aorta-to-femoral or femoral-to-proximal popliteal bypass, placement of crimped prosthetic tubes under very slight tension seems advantageous. In contrast, however, when the graft is carried below the knee, some redundancy in the lower portion of the tube should be allowed, since the anastomosis is performed with the knee flexed and it seems essential to avoid tension on the distal anastomosis even with the leg fully extended. There appears only one satisfactory anatomic path for the bypass tube, and that is through Hunter's canal into the popliteal

space and behind the popliteus muscle. The graft may be tunneled from the femoral incision to the anteromedial infragenual incision without difficulty and without an intermediate incision (Fig. 3). The same specially designed instrument used for the usual femoral-to-popliteal bypass serves well to make the tunnel and deliver the graft.

As has been previously pointed out, the range of technical error consistent with successful function becomes smaller the more peripheral restorative techniques are applied. In this connection, application of the bypass principle below the knee necessitates availability of a fine, nonfraying and technically easily worked fabric tube. The highly flexible crimped dacron tubes developed by us in co-operation with the Philadelphia Textile Institute have been found most reliable for technical performance of the bypass anastomoses. Experience has demonstrated that best results are obtained with a tube diameter 1.5 to 2 times the diameter of the distal artery to which it is attached.

The following 8 cases are presented briefly to show the variable application and pathologic circumstances in which extension of bypass operation below the knee appeared advantageous if not limb saving.

CASE REPORTS

CASE 1. C. M., a painter, 56 years old, was admitted to the Methodist Hospital on April 27, 1958, because of pain in the right leg. Two months previously he suddenly experienced pain while squatting.

Examination revealed all pulses in the right leg below the common femoral artery to be absent. Arteriographic studies demonstrated an abdominal aortic aneurysm and occlusion of the right superficial femoral and popliteal arteries (Fig. 4a and b).

On May 1, 1958, the abdominal aortic aneurysm was resected and replaced with a dacron bifurcation prosthesis. Limited distal lumbar sympathectomy was also performed. Through a low medial thigh incision a clotted popliteal aneurysm was excised. Because of the distal extent of this aneurysm, technical performance of the distal anastomosis was impossible through the distal thigh incision. Therefore, the posterior tibial artery proximal to the peroneal branch was exposed through an anteromedial infragenual incision and found satisfactory for graft anastomosis. Because of proximal propagation of the thrombus and extensive arteriosclerotic changes in superficial femoral artery, a common femoral to posterior tibial bypass was done with an 8 millimeter dacron tube (Fig. 4c).

FIG. 2. Photograph showing completion of end-to-side anastomosis between knitted dacron tube and distal popliteal artery.

Bounding dorsalis pedis and posterior tibial pulses were obtained on the right. The patient has resumed his previous occupation as a painter and remained well. On our advice, he has avoided extreme flexion of the right knee.

CASE 2. G. R., a retired businessman, 64 years old, began to experience cramping pains in his right leg 2 months before admission to Methodist Hospital on May 5, 1958. A pulsating mass was palpable in the right femoral area. The right popliteal, dorsalis pedis, and posterior tibial pulses were absent, and the right foot felt cooler than the left. Arteriography demonstrated an aneurysm of the right common femoral artery with occlusion of the superficial femoral artery (Fig. 5a and b). Extensive arteriosclerotic plaques were also evident in proximal portion of popliteal artery.

At operation, a low abdominal incision was made, and a tape placed about the right external iliac artery for proximal control. The aneurysm was excised through a femoral incision. A crimped dacron tube,

FIG. 3. Photograph showing incisions used in common femoral to distal popliteal artery bypass (Case 5). It is noteworthy that the graft in this case could be tunneled through Hunter's canal and behind the knee without an intermediate incision in spite of extensive scarring from previous injury and operation.

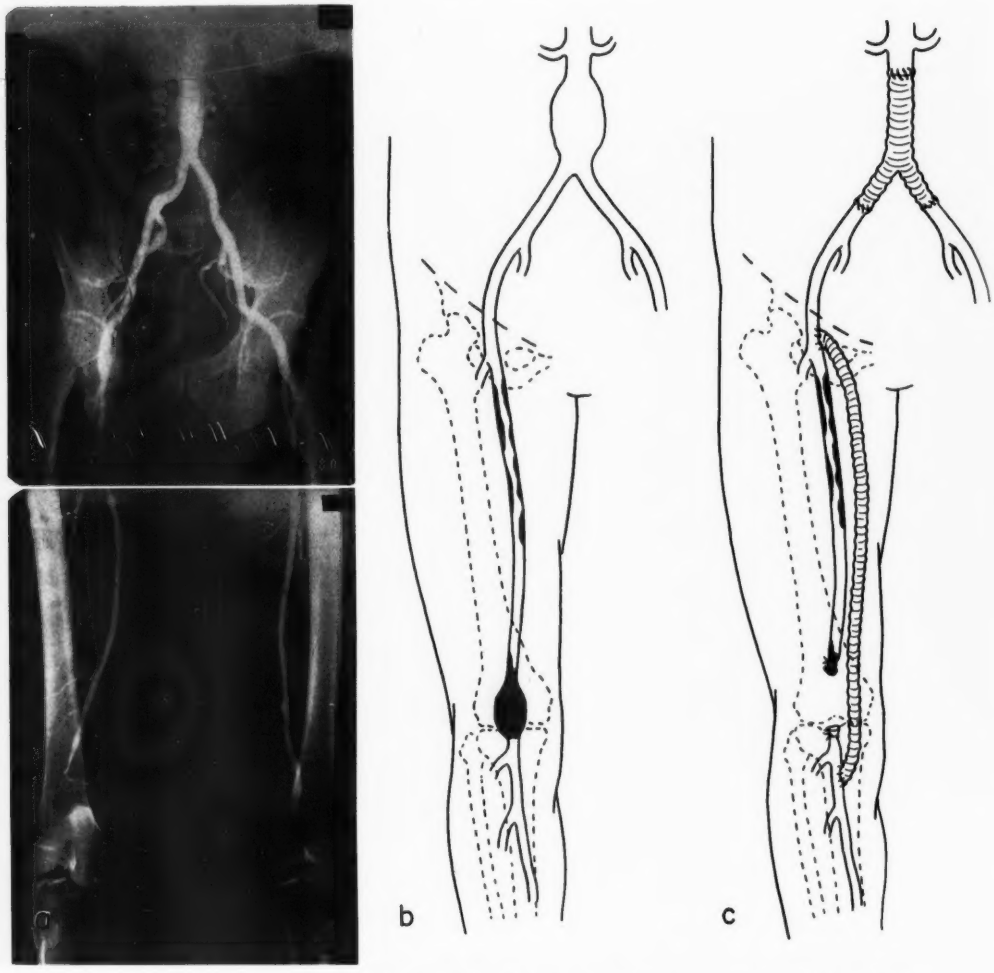

FIG. 4. a, Arteriogram in Case 1 demonstrating abdominal aortic aneurysm and occlusion of right superficial femoral and popliteal arteries. b, Drawing made from arteriogram showing location of aneurysms and extent of occlusive disease. c, Drawing showing method of surgical correction. An anteromedial infragenual incision facilitated graft anastomosis to side of the posterior tibial artery.

8 millimeters in diameter, was anastomosed to the terminal end of the external iliac artery. An incision made in the dacron tube opposite the origin of the superficial and profunda femoris arteries was used for anastomosis with this obliquely tailored bifurcation of the common femoral artery (Fig. 5c). Because narrowing and extensive arteriosclerotic disease in the upper and midpopliteal artery were observed on arteriography, an anteromedial infragenual incision was elected to expose the distal popliteal artery, and the dacron tube was brought through Hunter's canal into the popliteal space and anastomosed to the side of the distal popliteal artery below the knee. Right lumbar sympathectomy and incidental appendectomy were performed through the abdominal wound. Pedal pulses of excellent quality were restored and an arteriogram demonstrated a functioning bypass graft (Fig. 5d). The patient has remained asymptomatic since operation.

CASE 3. W. O., a salesman, 62 years old, began to experience claudications as well as rest pain in the left leg 3 months before admission to Methodist Hospital on May 17, 1958. Significant physical findings included an extremely weak left femoral pulse and

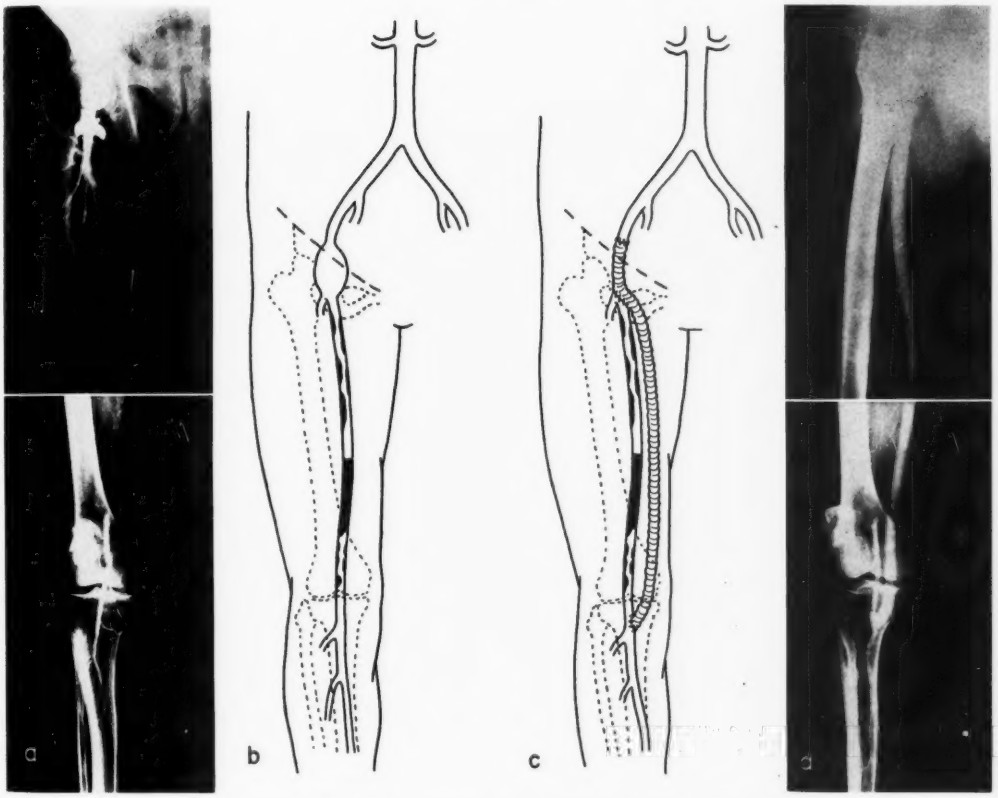

FIG. 5. a, Arteriogram in Case 2 shows aneurysm of common femoral artery, segmental occlusion of superficial femoral artery, and extensive arteriosclerotic disease of proximal popliteal artery. b and c, Drawings made from arteriograms showing location of lesions and method of surgical correction. d, Arteriogram after operation shows functioning arterial bypass below knee.

absence of palpable arterial pulsations below this level in the left leg. The left foot was decidedly cooler than the right and was pale. Arteriographic studies revealed extensive arteriosclerotic plaques in the terminal aorta and iliac arteries with almost complete occlusion of the left common iliac artery (Fig. 6a and b). The superficial femoral artery on the left was occluded and there were arteriosclerotic plaques with narrowing of the left proximal popliteal artery.

On May 21, 1958, thromboendarterectomy of the abdominal aorta and iliac arteries was performed through the transected common iliac arteries. After anastomosis of the iliac arteries, a small segment of the lumbar sympathetic chain was excised bilaterally at the sacral promontory, and incidental appendectomy was performed. Through a small femoral incision, an 8 millimeter crimped dacron tube was anastomosed to the side of the left common femoral artery. The tube was tunneled through Hunter's canal and the popliteal space into an anteromedial incision below the knee and anastomosed to the side of the terminal popliteal artery (Fig. 6c). Visible dorsalis pedis and posterior tibial pulses were obtained bilaterally and the patient has remained asymptomatic.

CASE 4. I. B., a 58 year old businessman, complained of cold feet and bilateral claudications of 2 years' duration. Failure of wound healing had occurred after bunionectomy of the right foot in September 1957. On physical examination, cool, pale feet and a small ulcer over the right first metatarsophalangeal joint were observed. Femoral pulses were palpable bilaterally but were definitely weakened; popliteal and pedal pulses were absent bilaterally. On arteriographic study, a small aneurysm of the abdominal aorta was demonstrated (Fig. 7a and b). The distal two-thirds of each superficial femoral artery was occluded, and the proximal portions of both popliteal arteries had an irregular outline suggestive of multiple arteriosclerotic plaques.

On May 28, 1958, an aortic aneurysm arising distal

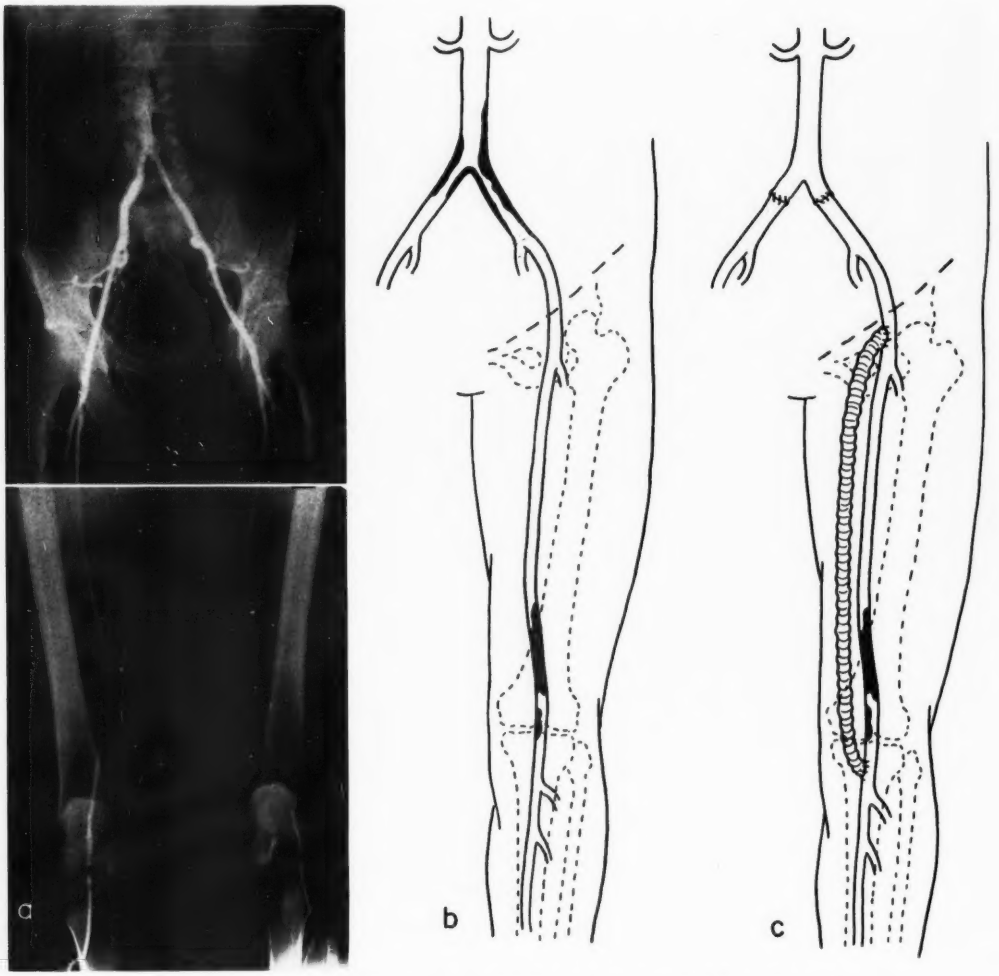

FIG. 6. a, Arteriogram in Case 3 showing partial obstruction of aortic bifurcation and occlusive disease of distal superficial femoral and proximal popliteal arteries. b, Drawing made from arteriogram showing extent of occlusive involvement. c, Drawing showing method of surgical correction. Thromboendarterectomy of aortic bifurcation was performed through transected iliac arteries. Femoral bypass was attached to distal popliteal artery below knee.

to the renal arteries was resected, and a crimped dacron bifurcation tube was anastomosed end-to-end proximally. The aortic bifurcation was closed with sutures as a blind proximal segment (Fig. 7c). The two limbs of the dacron tube were tunneled into the femoral region and anastomosed side-to-side to the common femoral arteries. Because of the extensive arteriosclerotic changes in the proximal left popliteal artery evident on arteriography, an infragenual anteromedial incision was used to expose its distal portion. At this level, the artery was well preserved. Accordingly, an 8 millimeter crimped dacron tube was extended by suture attachment to the distal end of the left limb of the bifurcation prosthesis below the side-to-side femoral anastomosis and was tunneled into the popliteal space and anastomosed to the side of the distal popliteal artery. On the right side, a medial thigh incision was used to expose the proximal popliteal artery, since it appeared to be affected by less significant arteriosclerotic disease. However, an endarterectomy was necessary prior to end-to-side anastomosis of the extended right limb of the bifurcation graft. The operation was completed

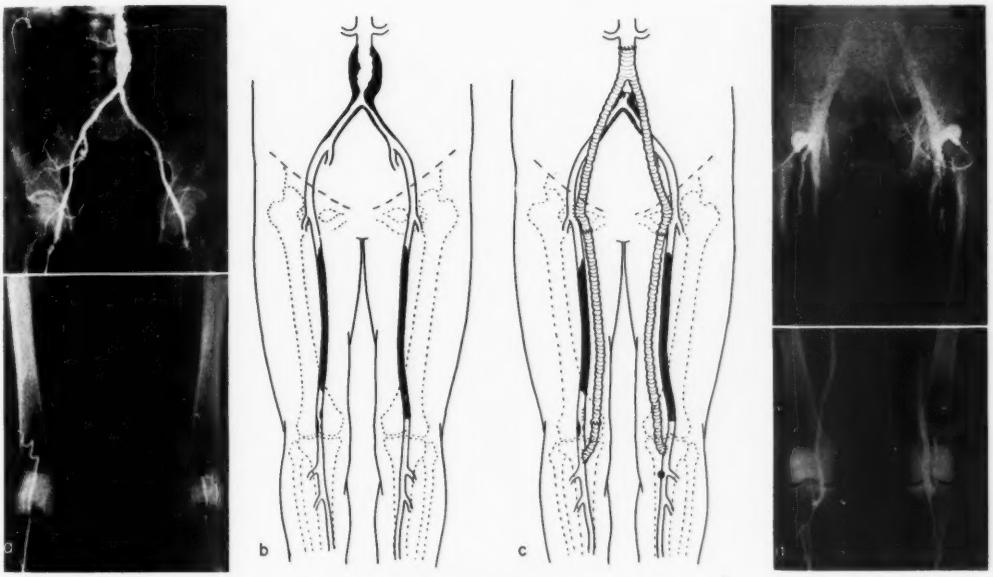

FIG. 7. a, Arteriogram in Case 4 showing abdominal aortic aneurysm and extent of femcropopliteal occlusive process. b, Drawing made from arteriogram showing location and extent of occlusive process. c, Drawing showing method of surgical correction. d, Arteriogram after operation showing functioning bypass grafts below knees.

with a bilateral low lumbar sympathectomy and appendectomy.

On the day after operation, pedal pulses were absent on the right, although they were bounding on the left. The right foot appeared in jeopardy at this time and so the right distal popliteal artery was exposed through an anteromedial infragenual incision. The vessel appeared well preserved at this level. The previous bypass tube below the profunda femoris was removed and the proximal arteriotomy in the popliteal artery was repaired. An 8 millimeter crimped dacron tube was attached to the right limb of the bifurcation prosthesis just distal to its side-to-side anastomosis with the common femoral artery. This tube was tunneled through Hunter's canal and the popliteal space and anastomosed to the side of the popliteal artery below the knee (Fig. 7c and d). Following this operation, bilateral pedal pulses of excellent quality have persisted, and the ulcer on the right foot has healed.

CASE 5. F. B., a 56 year old educator, was injured in an automobile accident in November 1950. After treatment and recovery from extensive fractures involving the right knee joint, he noted severe claudication in the right calf on walking. A right lumbar sympathectomy and stripping of the saphenous vein were performed elsewhere in 1952. In September 1957, in another city, an arterial homograft was inserted through an extensive posterior popliteal approach. An infection of the wound developed, necessitating the removal of the graft. The limb remained viable, but severe claudication persisted.

Arteriography demonstrated a block of the right superficial femoral artery in its middle third. Distally, the posterior tibial and peroneal arteries were demonstrable, with questionable evidence of a patent distal popliteal artery (Fig. 8a and b). On July 2, 1958, the distal popliteal artery was exposed through an anteromedial infragenual incision and was found to be patent. Accordingly, an 8 millimeter crimped dacron tube was anastomosed to the side of the right common femoral artery, tunneled through Hunter's canal into the popliteal space, and anastomosed to the distal popliteal artery. Postoperative recovery was uneventful, with restoration of dorsalis pedis and posterior tibial pulses (Fig. 8c and d.).

CASE 6. H. S., a 56 year old barber, experienced sudden excruciating pain in the right leg 3 hours before admission to Methodist Hospital on July 2, 1958. The right foot was anesthetic, with no venous filling. This patient had had a previous common femoral to proximal popliteal artery bypass for segmental occlusive disease of the superficial femoral artery in February 1957. A 5 millimeter braided nylon graft had been used.

At operation 7 hours after apparent occlusion of the bypass graft, a low medial incision was made in the thigh to expose the distal portion of the graft and proximal popliteal artery. Recent thrombus was re-

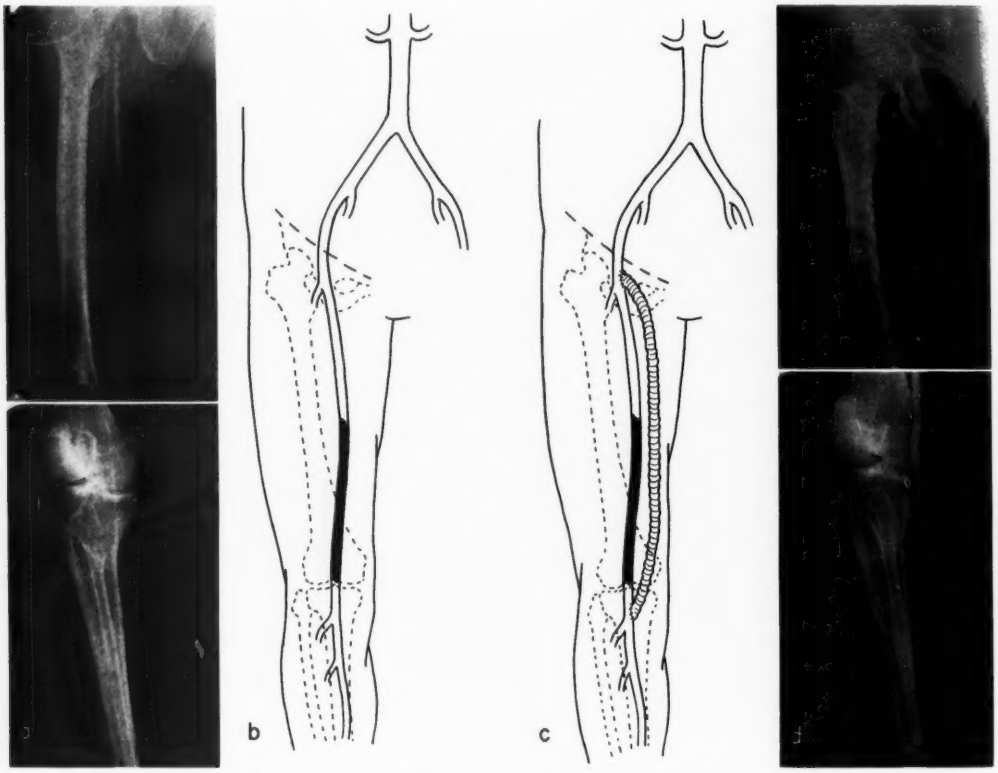

FIG. 8. a, Arteriogram in Case 5 showing extent of femoropopliteal occlusion. Anterior and posterior tibial arteries are visualized. Although patent, the distal popliteal segment is not seen. b and c, Drawings made from the arteriograms showing the extent of occlusive process and the method of surgical correction. d, Arteriogram after operation showing the functioning bypass graft below knee.

moved from the artery, but no backflow of blood could be obtained. Arteriotomy of the distal popliteal artery through an anteromedial infragenual incision facilitated removal of long propagated thrombi from the anterior and posterior tibial arteries with development of backflow from each artery (Fig. 9a). The nylon graft was removed with arteriorrhaphy at its attachments. An 8 millimeter dacron tube was anastomosed to the side of the proximal common femoral artery, tunneled through Hunter's canal into the popliteal space, and anastomosed to the distal popliteal artery below the knee (Fig. 9b and c). Dorsalis pedis and posterior tibial pulses were restored and anesthesia of the foot disappeared within several days. The patient has returned to work as a barber.

CASE 7. M. W., a 47 year old school teacher, had experienced increasing claudication of both legs for a period of 5 years. No pulses were found to be palpable in either leg below the common femoral artery. Arteriographic studies demonstrated bilateral occlusion of the superficial femoral artery (Fig. 10a and b). The occlusive process involved the left proximal popliteal artery.

At operation on July 10, 1958, common femoral artery to proximal popliteal artery bypass was performed on the right, utilizing an 8 millimeter crimped dacron tube. Attention was then directed to the left leg and after completing anastomosis of an 8 millimeter crimped dacron tube to the side of the left common femoral artery, the prosthesis was tunneled into an anteromedial infragenual incision and attached to the distal popliteal artery (Fig. 10c). Following operation, dorsalis pedis and posterior tibial pulses were palpable in each leg, and functioning bypass grafts were demonstrated by arteriography (Fig. 10d). The patient can now walk without claudication.

CASE 8. D. M., a retired businessman, 70 years of age, began to experience claudication in the left leg in

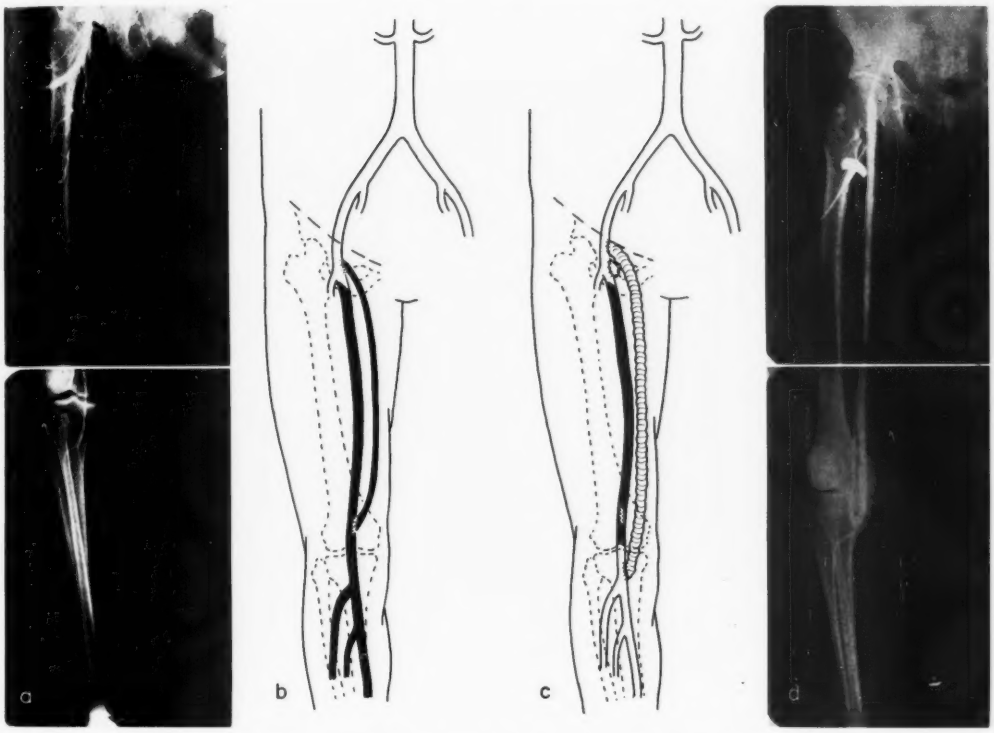

FIG. 9. a, Arteriogram of patient in Case 6 made before first operation showing segmental occlusion of the superficial femoral artery. b, Drawing showing the extent of thrombosis 18 months after the first bypass operation. c, Method of surgical correction with thrombectomy of the anterior and the posterior tibial arteries and arterial bypass below knee. d, Arteriogram after operation showing bypass graft.

1950. Left lumbar sympathectomy performed elsewhere in 1953 provided only transient relief. Claudication also developed in the right leg and in October 1956 a bilateral common femoral to proximal popliteal artery bypass was performed by using braided crimped nylon tubes. In June 1957 the right femoral bypass thrombosed and was replaced by a crimped dacron tube with end-to-end anastomosis to the proximal popliteal artery. In April 1958 the left nylon graft thrombosed and a left femoropopliteal dacron bypass was attached above and below the old prosthesis. Unfortunately, a wound infection developed with secondary hemorrhage necessitating removal of the graft. The femoral and popliteal wounds were allowed to heal by second intention but gangrenous changes developed in the superficial aspect of the toes and heel of the left foot.

On July 10, 1958 the distal popliteal artery was explored through an anteromedial infragenual incision. After removal of a small thrombus, excellent back bleeding was obtained. To avoid the old femoral incision which was incompletely healed, an 8 millimeter crimped dacron tube was attached to the external iliac artery through an extraperitoneal left lower quadrant incision. This tube was then tunneled without great difficulty through the adductor canal into the distal popliteal space and anastomosed to the side of the distal popliteal artery (Fig. 12a and b). Since operation, the bypass has functioned well, and the areas of superficial necrosis on the foot have desquamated and been replaced by pink epithelium.

Since these operations were performed, 25 additional patients have been operated upon by this method. Late thrombosis occurred in 10 of these 33 cases. Reoperation was performed in 6 patients with successful thrombectomy and graft replacement in two. Thus, in 25 (76 per cent) of these 33 patients the bypass grafts are still functioning with

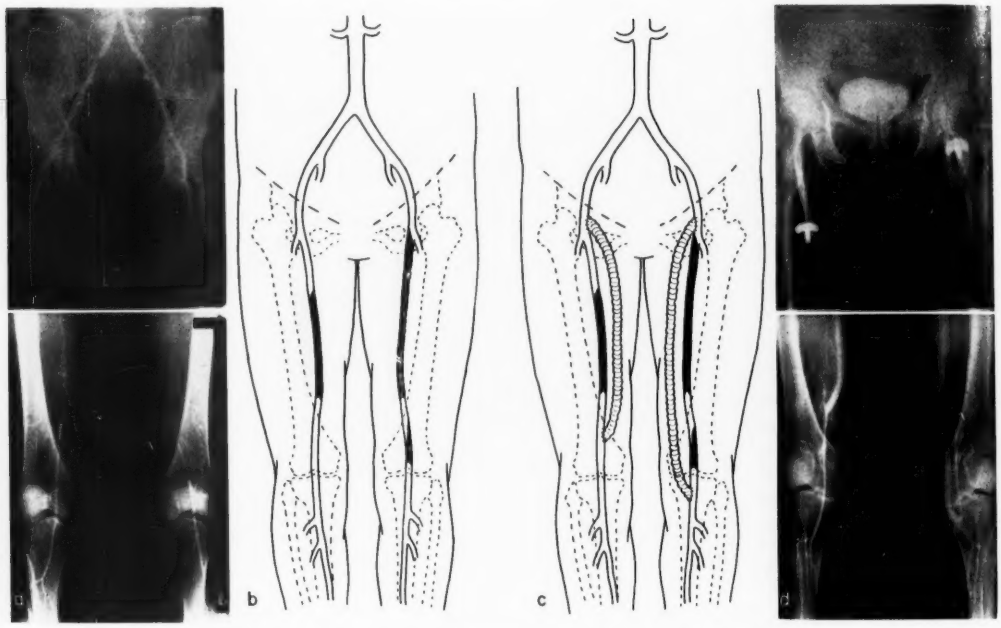

FIG. 10. a, Arteriogram in Case 7 showing segmental occlusion of right superficial femoral artery and more extensive involvement of left superficial femoral and popliteal arteries. b, Drawing made from arteriogram showing extent of occlusive process. c, Drawing showing method of surgical correction with bypass grafts. d, Arteriogram made after operation showing bypass graft to proximal popliteal artery on right and distal popliteal on left side.

palpable pedal pulses. Amputation has been necessary in only 1 instance and this particular patient had pre-existing gangrene of the foot.

DISCUSSION

Previous experience has shown that the obstructing lesion in chronic arteriosclerotic occlusive disease below the aortoiliac level also tends to be segmental in character and involves most frequently the superficial femoral artery. The extent of the obstruction, however, is variable. Although the standard femoral and medial distal thigh incisions serve satisfactorily in most instances for femoral artery bypass, in occasional patients legs may be salvaged or better results obtained if the distal popliteal or posterior tibial artery is used for the distal anastomosis. The anteromedial, below-the-knee approach to the main arterial channel offers a sound anatomic and surgical extension of the bypass principle in certain instances.

Although well recognized pathologic forms of both aortoiliac and femoral occlusive disease, in terms of localization and extent, are now established, combinations of these occlusive patterns as well as coexisting aneurysms are not infrequent. The variability of the pathologic combinations are well illustrated in the 8 cases reported here that demonstrate the applicability of bypass below the knee.

Developmental anatomy and anatomic variations of the popliteal artery were extensively studied several decades ago by Senior. We have observed many different anatomic arrangements of the popliteal artery in relation to the origin of the anterior tibial, posterior tibial, and peroneal arteries (Fig. 11). In every instance, however, the main arterial channel below the knee has

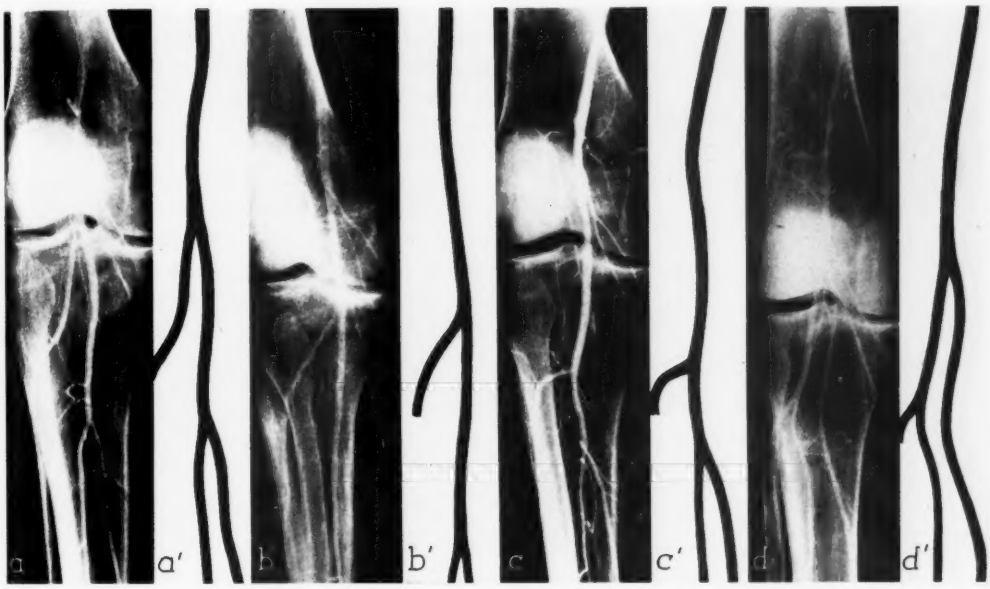

FIG. 11. Arteriograms and diagrams showing anatomic variations of principal arteries below knee. a and b, Demonstration of high origin of anterior tibial artery. In such instances the posterior tibial artery would be used for graft attachment below knee. c, Most common anatomic arrangement. d, Unusual anatomic variation showing anterior tibial and peroneal arteries arising above knee from common trunk.

been easily accessible through the anteromedial infragenual approach. In this connection it has been interesting for us to note the paucity of small collateral branches arising between the knee and the transverse bridge of the soleus muscle (Fig. 13). This fortunate arrangement offers certain advantages to the vascular surgeon. For one thing the artery can be easily mobilized and brought superficially for ease in technical performance of the operation. For another, such an approach produces minimal trauma and few, if any, collateral vessels need to be sacrificed.

Some concern may be given the possibility of graft kinking when spanning such a mobile joint as the knee. For this reason, all such patients have been instructed not to flex the knee beyond 90 degrees. Patients with occlusive disease or popliteal aneurysm, however, are in the older age groups, and such limitation in activity offers no significant handicap.

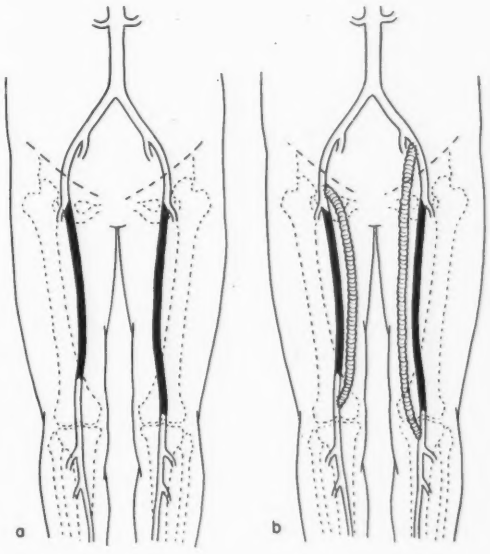

FIG. 12. a, Drawing showing occlusive lesions in Case 8. b, Drawing showing arterial bypass grafts following operation.

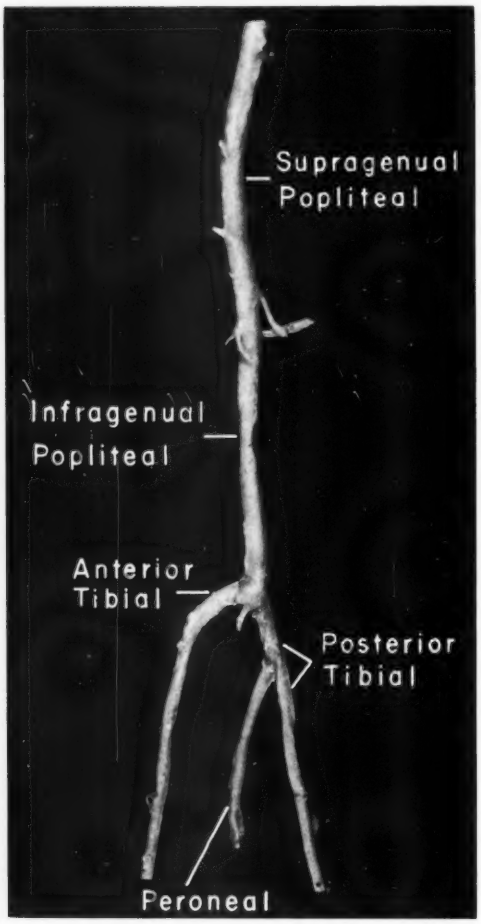

FIG. 13. Photograph of popliteal artery specimen with its branches. Note absence of small branches arising from infragenual segment of popliteal artery.

SUMMARY

Restoration of pulsatile blood flow in the lower leg is the objective of surgical treatment for segmental occlusive disease of the femoral artery. This objective has been reached in 86 per cent of 317 patients treated by the bypass graft technique.

The proximal popliteal artery is usually suitable for distal bypass anastomosis. Satisfactory exposure of the proximal popliteal artery can be accomplished through a medial thigh incision in conjunction with a femoral incision.

In certain instances the proximal popliteal artery may be unsatisfactory for the distal bypass anastomosis because of arteriosclerotic occlusive disease or aneurysm. Exposure of the distal popliteal artery through a medial thigh incision is difficult and posterior approach to the popliteal artery is awkward in conjunction with femoral or abdominal incisions.

The distal popliteal artery may be easily approached through an anteromedial incision below the knee. This incision may be made with the patient supine, in combination with femoral and abdominal incisions. No transection or splitting of muscle or tendon is required and few, if any, collateral vessels are sacrificed.

The only satisfactory anatomic path for the bypass tube from the common femoral artery to the infragenual portion of the popliteal artery is through Hunter's canal into the popliteal space and behind the popliteus muscle. The bypass tube can be tunneled between these points without difficulty and without an intermediate incision.

Nine instances in which below-the-knee arterial bypass has been used in 8 patients are presented to illustrate the variable application and pathologic circumstances in which this operation appeared advantageous.

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THE EFFECT OF HYPOTHERMIA AND STEROID THERAPY ON EXPERIMENTAL CEREBRAL INJURY

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IT HAS BEEN SHOWN by Williams and associates that hypothermia favorably affected cerebral changes associated with interruption of total body circulation of blood in the dog. It was decided, therefore, to determine if hypothermia would influence the course of other types of cerebral damage. Since the use of prednisolone and cortisone leads to improvement in patients with cerebral neoplastic metastases, and since this has been attributed in part to reduction of cerebral edema, it was also decided to test this form of therapy, both alone and as an adjunct to hypothermia.

Lethal cerebral lesions were produced in 4 series of rabbits. Three groups were treated by the methods mentioned, the fourth serving as a control. It was found that only a combination of both methods of therapy produced a significant decrease in mortality.

REVIEW

A quantitative method described by Hass and Taylor employing focal freezing through the intact skull for production of closed cerebral lesions in rabbits was used. Briefly, this consisted of the application of a metal disc cooled by carbon dioxide to the exposed intact skull of anesthetized animals. The effective depth of the negative thermal gradient was determined by the duration of contact and the diameter of the cooling plate. This procedure produced a circumscribed area of hemorrhagic destruction in the underlying brain (Fig. 1). Histologic examination revealed neuronal degeneration, congestion, edema, and perivascular hemorrhage within the limits of the lesion. With larger animals, edema in the contiguous white matter was also conspicuous. The volume of the lesion was estimated by measurements of the surface area and depth, and the volume of the brain by Archimedes' principle. The extent of damage was then expressed as the volume of lesion per 100 milliliters of brain. It was found that rabbits with more than 18 per cent cerebral damage always died. In order to obtain this much damage, it was necessary to make lesions in both cerebral hemispheres.

By spacing 2 lesions at different time intervals in the same animal, it was shown that lesions produced within a 24 hour interval had the same lethal effect as lesions produced simultaneously. The average survival time for simultaneous lethal lesions was 5 hours (S.D. = 1.2, n = 9). On the other hand, lesions produced at 48 hour intervals, with total damage exceeding 18 per cent, showed a significant increase in survival rate.[1] From this observation it was concluded that the lethal factor associated with these lesions acted for at least 24 hours or that recovery mechanisms began to operate after this time.

One group of animals was then treated with intravenous hypertonic glucose and another with surgical decompression over the lesions. The former treatment was with-

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Dr. Clasen, Postdoctoral Research Fellow, National Institute of Neurological Diseases and Blindness, United States Public Health Service.

[1]Five of 12 survived as compared to 0 of 17 with simultaneous lesions, including the animals in this series. For these figures, $P < 0.05$.

TABLE I.—DURATION OF LIFE OF ANIMALS DYING OF CEREBRAL INJURY

Control			*Prednisolone*			*Hypothermia*				*Hypothermia and prednisolone*			
Exp. No.	*Survival time, hrs.*	*Volume of damage, c.c./100 c.c. brain*	*Exp. No.*	*Survival time, hrs.*	*Volume of damage, c.c./100 c.c. brain*	*Exp. No.*	*Survival time, hrs.*	*Volume of damage, c.c./100 c.c. brain*	*Body temp., ° C.*	*Exp. No.*	*Survival time, hrs.*	*Volume of damage, c.c./100 c.c. brain*	*Body temp., ° C.*
56	2.5	20.00	45	2.5	21.36	6	27	18.26	25.0	20	30	21.62	26.0
57	3.0	18.76	46	3.2	20.26	8	32	19.54	26.0	22	48	19.00	26.0
58	2.8	18.98	48	2.5	20.56	9	29	21.26	25.5	27	20	18.70	26.0
59	3.2	19.68	49	3.0	19.84	10	12	20.26	26.2	31	20	21.69	25.0
60	3.0	18.18	50	3.0	21.00	11	28	21.46	27.5	36	24	21.00	25.0
61	2.5	20.56	51	3.0	20.46	13	26	21.00	28.0	39	18	22.30	23.5
62	2.5	21.76	52	2.2	19.86	15	22	19.36	25.5	40	16	23.22	28.5
63	3.0	18.46	53	3.2	19.26	18	17	20.44	27.0	43	24	23.42	25.0
			54	3.0	20.20	19	27	21.70	27.5	44	22	23.00	26.0
			55	2.0	20.68	33	20	21.36	27.5				
						37	32	19.20	28.0				
						41	26	20.22	28.0				
x	2.8	19.55		2.7	20.35		25	20.34	26.8		25	21.55	25.7
sx	0.1	0.42		0.14	0.19		1.7	0.31	0.32		3.2	0.57	0.44
t*							5.02				6.51		
p†							< .001				< .001		

*Comparison with the control group given the same anesthetic.
†The hypothesis tested is that the means differ irrespective of the variances. Approximately one-half of the degrees of freedom were used in determining the probability level.

out therapeutic effect, but with the latter some animals survived as much as 30 per cent cerebral damage.

METHODS

Lethal lesions were produced in rabbits as previously described by Hass and Taylor. The anesthetic was nembutal (50 mgm./3 kgm. of body weight) given intravenously. Each rabbit was also given 0.25 milligram of chlorpromazine and 0.25 milligram of promethazine in another vein immediately after the nembutal. These served as thermoregulatory center blocking agents. All animals were anesthetized in this manner whether they were to be subjected to hypothermia or not.

TABLE II.—MORTALITY IN THE TREATED AND UNTREATED GROUPS

	No. of animals	*No. surviving*	*No. dying*	*Per cent surviving*	*p†*	*Significance*
Untreated	17	0	17	0	—	—
Prednisolone	11	1	10	9.1	0.393	N.S.
Hypothermia	12	0	12	0	1.000	N.S.
Prednisolone and hypothermia	14	5	9	28.0	0.047	S
Hypertonic glucose*	8	1	7	12.5	0.320	N.S.
Surgical decompression	12	4	8	33.3	0.021	S

*From previously published data of animals with 18.3 to 24.7 per cent of damage.
†Fischer's exact test used. Critical level=0.05.

The animals were divided into 4 groups. The first group consisted of 8 animals and served as a control. The second group consisted of 11 animals which had received 25 milligrams of prednisolone acetate on the day prior to production of the lesion and the same dosage daily thereafter. The third group was composed of 12 animals which were subjected to hypothermia before receiving the cerebral lesion. Hypothermia was induced by immersing the anesthetized animal into an ice bath for approximately 50 minutes. The body temperature was measured by a thermometer inserted about 10 centimeters into the rectum. The body temperature dropped about 1 degree C. per 5 minutes in the ice bath and fell another 1 to 3 degrees C. after removal from the ice bath. The return to normal body temperature was spontaneous and gradual, apparently proceeding with the animal's recovery from anesthesia. The fourth group consisted of 14 animals with combined hypothermia and steroid therapy as indicated previously.

All animals were observed postoperatively and the time of death recorded. The animals were not evaluated neurologically. They were observed hourly during the day and at least every 6 hours during the night. When an

animal was found dead, the survival time in hours was counted up to the last time it was seen alive. The time was measured from the moment of infliction of the first lesion. For the reasons previously mentioned, animals which lived more than 48 hours were considered as survivors. These animals were sacrificed after 72 or 96 hours. The volume per cent of cerebral damage was determined in all animals as indicated.

RESULTS

The results are given in Tables I and II. The statistical analysis was done by Mr. Sylvanus Tyler of the Argonne National Laboratory, Lemont, Illinois. There was no statistically significant difference between the extent of damage in the various groups or in the degree of hypothermia in the two groups subjected to this procedure. Since there were no survivors in the control group, it was concluded that the use of nembutal and the blocking agents, rather than ether, for anesthesia did not influence the mortality for lesions of this size. Therefore, animals from the previous series with lesions of comparable size were added to the control group for computation of survival rates. There were 9 such animals with a mean lesion volume of 21.4 per cent (S.D. = 1.5). The combined control group consisted, therefore, of 17 animals with no survivors.

As shown in Table II, neither prednisolone nor hypothermia, when used alone, produced significant decrease in mortality. Hypothermia, however, markedly prolonged the survival time as shown in Table I. Hypothermia and prednisolone used in combination produced both an increased survival time in animals dying of cerebral injury and a decrease in mortality in the group as a whole. The increase in survival time, however, was no greater than that with hypothermia alone.

For purposes of comparison, previously published data on effects of intravenous hypertonic glucose and surgical decompression were included in Table II. As mentioned previously, the former was ineffective while the latter was effective in reducing mortality associated with these lesions. Thus, there were two methods by which these animals were effectively treated, namely, surgical decompression or prednisolone with hypothermia. These seemed equally effective for the apparent difference in mortality was not statistically significant (using Fischer's exact test, $P = 0.613$).

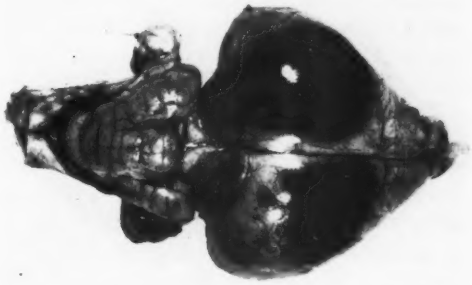

FIG. 1. Gross appearance of bilateral freezing lesions in the rabbit brain.

DISCUSSION

Previous experience with the therapy of these lesions indicated that mortality could be significantly reduced by surgical decompression. Such a procedure might be expected to relieve both increased intracranial pressure and subcortical anatomic distortion. In the present series of experiments, two nonsurgical procedures are evaluated, steroid therapy and hypothermia. These were instituted prior to the production of the lesion. The effect of hypothermia on the brain of the dog has been studied by Rosomoff. He showed that a state of hypothermia in this animal is associated with a decrease in systemic blood pressure and pulse rate accompanied by a decrease in cerebral blood flow and oxygen consumption (10). There was also a decrease in brain volume and in cerebrospinal fluid pressure paralleled by a decrease in the systemic venous pressure (9). These findings suggest that hypothermia might be an effective means for preventing or treating cerebral swelling. While the production of

cerebral lesions in hypothermic rabbits resulted in an increased survival time, there was no significant decrease in the mortality of the treated group as a whole. The latter was only achieved, however, when prednisolone was utilized in conjunction with hypothermia.

These experiments were not primarily designed to elucidate mechanisms of effects of therapy on cerebral injury. However, certain ideas may be formulated. First of all, from a morphologic viewpoint there were at least three important changes associated with these cerebral lesions: cellular destruction, hemorrhage, and edema. Damaged cells may release toxic substances into the surrounding tissues. For the central nervous system, serotonin may play a role in this mechanism since this is present in relatively high concentrations in brain tissue, has been found in the cerebrospinal fluid of some patients with head injuries, and when injected into the subcutaneous tissues produces a greater degree of edema than histamine. Free acetylcholine has been demonstrated in the spinal fluid of animals subjected to experimental cerebral trauma and in some human cases of head injuries. This observation is a basis for the use of atropine in treatment of head injury. Acetylcholine is a vasodilator and increases the permeability of the blood brain barrier so that it may also play a role in the present experiments. The fact, however, that the animals were benefited by simple decompression indicates that if these factors played a role in the death of the animals, it was a secondary one. The primary factor was probably the acute space-consuming effects of hemorrhage and edema. The mean survival time of 2.8 hours in the controls indicates that hemorrhage was more important than edema in producing death from large lesions since the latter probably requires a greater time interval for its development.

The ineffectiveness of intravenous hypertonic glucose in the treatment even of smaller lesions (with longer survival times) may be explained by reference to physiologic studies made by Clasen and associates on dogs with similar lesions (1–3). It was found that these lesions were associated with a persistent elevation of intracranial pressure and that this pressure could be reduced, at least temporarily, by intravenous hypertonic glucose. However, this treatment failed to reduce the water increment in the damaged hemisphere. From this it was concluded that the decrease in the intracranial pressure was due to absorption of cerebrospinal fluid from the central nervous system generally rather than to selective absorption of fluid from the damaged hemisphere.

Rosomoff has shown that hypothermia afforded protection against infarction due to severance of the middle cerebral artery, provided the hypothermia was induced within 15 minutes from the time the artery was severed (7). More recently, he has conducted experiments in dogs using a modification of our technique for freezing the brain, and found that there was about an 8 per cent increase in volume of the damaged hemisphere in the first hour (8). This was followed by a slower, progressive weight gain which reached 24 per cent in 16 hours. The first increase was attributed to the outpouring of blood and fluid into the areas of damage and the second to the development of swelling in the damaged hemisphere. Hypothermic animals failed to show this second volume increase, even when observed for as long as 36 hours. Hypothermia had no measurable effect on lesion size. Histologically, the lesions in the hypothermic animals showed less evidence of cellular injury, a reduction in interstitial edema, and a marked decrease in hemorrhage and vasodilatation when compared with the normothermic controls. As with our rabbits, hypothermia in these dogs increased the survival time but did not significantly decrease the mortality. If similar gross and microscopic changes may be assumed for the rabbits, then the increase in survival time may be attributed to a

decrease in hemorrhage and edema probably as a result of the systemic hypotension accompanying hypothermia.

The action of cortisone and related substances such as prednisolone on inflammation in peripheral tissues is well known. Study of action of corticoids on the central nervous system and cerebral edema is much less complete. We have been unable to find quantitative data on the subject, though qualitative studies dealing mainly with cellular changes in the later stages of injury have been published. Prados and associates (5, 6) exposed the brains of cats to air. Some animals developed gross swelling of the exposed hemisphere. Trypan blue was injected intravenously at the conclusion of the exposure. This injection resulted in a diffuse staining of the whole brain, the exposed area being more intensely stained. This staining was not observed in control brains. Animals receiving adrenal cortical extract prior to exposure showed practically no staining. An excessive dose of the extract and use of the adrenotropic factor of the pituitary seemed to produce the opposite effect. In any case, the relationship between this mild form of cerebral injury and the reaction accompanying large areas of tissue necrosis is not known. In spite of the lack of quantitative data on the subject of cerebral edema and cortisone, the hypothesis that cortisone depresses the edema is perhaps defensible. In our animals, the survival times of the control and prednisolone treated groups indicated that hemorrhage was a more important factor than edema in the mortality associated with large lethal lesions. This observation could explain the failure to observe any decrease in mortality with prednisolone. If the hypothesis is correct, then a beneficial effect should be observed with smaller lesions which have a longer survival time and in which cerebral edema is presumably a more important factor.

The mechanism of action with the combined form of therapy is obscure. The beneficial effect of prednisolone in this case cannot be ascribed to a depression of cerebral edema since we have no evidence that there was a progressive space-consuming lesion in the hypothermic rabbits, and the data of Rosomoff (8) on dogs under similar conditions suggest that there was not. Whatever the mechanisms by which a combination of hypothermia and prednisolone decreased the mortality in these animals, the fact remains that it did so. It must be remembered, however, that these animals were pretreated and it does not necessarily follow that the measures would be effective if instituted after the production of the lesion. Hypothermia is being used in clinical trials in treatment of head injuries and apoplexy. If it is found to be effective, our experimental results are an indication that the addition of prednisolone to the hypothermal regimen should increase its effectiveness.

CONCLUSIONS

The effect of prednisolone and hypothermia upon acute closed cerebral lesions in the rabbit was studied. It was found that a combination of the two methods of therapy instituted before the lesion was produced gave a significant decrease in mortality and an increase in survival time in those animals which died. Hypothermia alone gave only the latter effect.

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STUDIES IN METABOLISM OF TRAUMA

III. Postoperative Sodium Retention

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IT HAS LONG BEEN RECOGNIZED that one of the metabolic changes in man following trauma concerns the handling of sodium. If a normal person is on a low sodium intake, a maximal reabsorption of sodium will take place in the proximal tubules of the kidney and, after 2 to 3 days of decreasing negative sodium balance, he will excrete practically no sodium in the urine and be in zero balance in regard to sodium. If the sodium loss is replaced at this point, he will start to excrete sodium in a normal way. If, however, the low sodium intake is of longer duration, the pattern changes, that is, after resuming a normal sodium intake, the kidney will continue the sodium conservation in excess of replacement, thus leading to a positive sodium balance.

A subject exposed to trauma will, in regard to the urinary handling of sodium, behave like a normal person on a prolonged low sodium intake, in that he may lose sodium on the day of trauma but then conserve it regardless of intake. As long as no fluid therapy is required, this will not represent any problem because the patient is conserving his sodium at a time when no intake is available.

If fluid replacement is necessary to maintain blood pressure and blood volume, difficulties are often encountered when the organism begins to mobilize edema fluid and, because of sodium retention, is unable to excrete the water. It is a well established fact that the kidneys' preservation of sodium through an increased reabsorption of sodium also leads to water retention. But, besides the sodium conservation, other factors are at work during trauma. The trauma releases, presumably neurogenically, antidiuretic hormone (ADH) from the posterior pituitary which promotes water reabsorption from the distal tubules or collecting ducts in the kidney and even without sodium retention the patient is faced with water retention if excess fluid is given.

Water retention may result in a weight increase, causing a dilution of the patient's electrolytes. Such an increase in weight can be due only to water retention as the caloric intake usually is, at best, far from adequate the first days after the trauma. The dilution may be caused entirely by the water retention, but other causes have been suggested, as will be discussed later.

Apparently at least two mechanisms are simultaneously involved in the posttraumatic homeostatic regulations of sodium and water in man. To determine whether they are independent or interdependent, it might be of value to study one thing at a time. In previous articles (6, 7) it has been shown that, by supplying the organism with solute/water in the ratio in which solutes/water are found in the urine, homeostasis is maintained in a period when antidiuresis is prevailing.

A group of young men and women on no oral intake, on bed rest, and given intravenously 1,500 to 1,600 cubic centimeters of 5 per cent dextrose in water per square meter surface area, in 24 hours lost 1,600 to 2,000 grams and 700 to 1,200 grams, respectively,

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TABLE I.—SERUM AND WEIGHT CHANGES ON DAY OF OPERATION

	Group 1 *18 patients*	*Group 2* *29 patients*
Weight change, gm.	−164 ±226	−1164±173
Change of corr. serum osm., per cent	−3.51±0.69	−0.07 ±0.55
Change of serum sodium, per cent	−3.78±0.77	−0.18 ±0.62

Group 1 patients were given 5 per cent dextrose in water on the day of operation.
Group 2 patients were given 4 per cent urea in the intravenous fluids on the day of operation and the first postoperative day.

and their serum electrolytes remained unchanged. Given pitressin and the same amount of fluid, normal controls gained in weight and their serum electrolytes became diluted as in patients in the postoperative period. If 4 per cent urea was added to the infusion, however, the subjects lost weight and maintained their electrolyte concentrations just as normal controls without antidiuresis. It was found feasible to maintain homeostasis and avoid water retention in patients with normal or nearly normal kidney function by supplying them with solutes to overcome the antidiuresis, either with a 4 per cent urea solution or a protein intake that amounted to the same concentration of urea.

This study was undertaken to see if sodium retention is present postoperatively when water retention is prevented by the establishment of an osmotic diuresis with 4 per cent urea.

TABLE II.—SERUM AND WEIGHT CHANGES ON THE FIRST THREE POSTOPERATIVE DAYS

	*Group 1**	*Group 2†*
1st postop. day		
Weight, gm.	−438 ±220	−730 ±228
Corr. osm., per cent	+0.23±0.87	+0.90±0.93
Serum Na, per cent	+0.86±0.76	−0.38±0.79
2nd postop. day		
Weight, gm.	−241 ±227	+49 ±201
Corr. osm., per cent	+1.28±1.01	−1.08±0.89
Serum Na, per cent	+1.22±0.98	−0.50±0.87
3rd postop. day		
Weight, gm.	−31 ±245	+90 ±205
Corr. osm., per cent	+1.38±1.72	−1.23±1.40
Serum Na, per cent	+2.98±1.73	+0.40+1.91

Group 1 patients were given 5 per cent dextrose in water on the day of operation. Group 2 patients were given 4 per cent urea in the intravenous fluids on the day of operation and the first postoperative day, but no patient in either group had urea on the second and third postoperative days.
The patients in the two groups had the same intake of calories, sodium chloride, and potassium.
*First postoperative day, 15 patients; second postoperative day, 11 patients; third postoperative day, 7 patients.
†First and second postoperative days, 14 patients; third postoperative day, 10 patients.

METHODS AND MATERIAL

All of the patients were on a complete balance study in regard to sodium, potassium, chloride, nitrogen, and water for 4 days postoperatively. They all were studied in 24 hour periods at the beginning and end of which they were weighed on a bed scale following urination. Weighing was done at 9 a.m., at which time blood was drawn for chemistries. The analysis of urine and serum has been carried out by the same methods as in previous studies (6, 7). As this study is concerned only with the days immediately following trauma, the amount of feces was negligible and no determinations of the loss through feces have been made. Gastric suction and bile drainage have been analyzed as the urine. All the balance figures have been corrected to 1.73 square meter surface area.

From the standpoint of intravenous therapy, the patients were divided into two groups: (1) a control group of 18 patients treated with approximately 2,100 cubic centimeters of 5 per cent dextrose in water intravenously on the day of operation; (2) a group of 29 patients exposed to surgery comparable to group 1, but to whom in the first 2 postoperative days about 3,000 cubic centimeters of 5 per cent dextrose in water with 4 per cent urea were given intravenously. Some of these patients were given additionally around 80 milliequivalents of sodium chloride. Results from the study of some of the patients in groups 1 and 2 have been published earlier (6, 7).

RESULTS

In Table I are presented the means and standard deviations of changes in weight, serum osmolality,[1] and serum sodium for the day of operation, the last two of which are expressed as the percentage variation from day to day. The serum osmolality is corrected for the increase in concentration

[1]Millimols per liter of water.

TABLE III.—SODIUM BALANCES ON THE DAY OF OPERATION AND THE FIRST THREE POSTOPERATIVE DAYS

	Group 1			Group 2		
	Intake	*Output*	*Balance*	*Intake*	*Output*	*Balance*
Day of operation	0±0	54.2±10.8	−54.3±12.6	62.4± 9.2	95.0+8.5	−32.6± 9.9
1st postoperative day	56.8±15.1	34.1± 9.7	+22.6±16.1	64.1±15.1	59.6±9.7	+ 4.6±23.5
2nd postoperative day	79.9±15.1	23.8± 9.3	+56.1±14.9	39.5±13.3	38.1±8.2	+ 1.4±13.2
3rd postoperative day	58.9±16.8	24.3± 7.6	+34.6±13.0	44.2±12.8	29.5±5.8	+14.7± 9.6

The figures represent mean± standard deviation of sodium intake, output, and balance in milliequivalents.
Group 1 patients were given 5 per cent dextrose in water on the day of operation. Group 2 patients were given 4 per cent urea in the intravenous fluids on the day of operation and the first postoperative day, but no patient in either group had urea on the second and third postoperative days.
On the day of operation, group 2 patients had significantly higher sodium intake and output. The balance was not significantly different from group to group. On the first postoperative day, no significant difference between the two groups. On the second postoperative day, the intake was higher and the balance positive in group 1, while the output was not significantly different from group to group. On the third postoperative day, there was no significant difference between the two groups.

due to increase in blood urea nitrogen, as this does not reflect any real change in the extracellular to intracellular concentration ratio since urea is distributed over total body water. Thus calculated, it can be seen that the corrected serum osmolality is varying very closely to the serum sodim concentration.

On the day of operation, the weight change in the patients in group 1 was not significantly different from the preoperative weight, while the patients in group 2 had a weight decrease close to the decrease found in a normal person receiving 2,000 cubic centimeters of dextrose in water intravenously in a 24 hour period. It is also seen that, while the serum sodium decreased 3.8 per cent in the patients in group 1, the serum values were unchanged from the preoperative values in the patients in group 2.

In Table II are presented the means and standard deviations of changes in weight, serum osmolality, and serum sodium for the first 3 postoperative days. It can be seen that, while the patients in both groups lost weight on the first postoperative day, the difference was not significant. Two of the patients in group 2 (Nos. 179, 191) did not receive urea on the first postoperative day. However, because of urea retained from the day of operation, they had solutes enough to maintain a good diuresis with corresponding decrease in weight and, for this reason, were included in the group of patients that got urea. There was no significant difference between the weight changes of the patients in either group on the second and third postoperative days. It may be remembered that no urea was given to any of the patients on the second and third postoperative days. Also, the caloric intake as well as water intake (Figs. 1 and 2) was the same for the two groups. The serum osmolality and the serum sodium changes were not different, either from each other or from zero.

In conclusion, it can be stated that no significant change in serum osmolality or serum sodium took place in the patients in group 2, all of whom received urea. In contrast, the patients who did not receive urea (group 1) showed a significant drop in serum sodium and serum osmolality on the day of operation, but no changes in the following 3 days. The implication here is that, while the patients in the urea group (group 2) had no change in serum sodium as a result of surgery, those in the control group showed a drop and serum sodium remained low for the 4 days they were observed.

Table III shows the means and standard deviations of sodium intake, sodium output, and sodium balance for both the control group (group 1) and the urea group (group 2) on the day of operation and the 3 following days. The greatest difference appears on the day of operation, when the patients in the urea group had a mean sodium intake of 62 milliequivalents, with a mean output of 95 milliequivalents, while the patients in the control group, on a mean zero intake, had a mean output of 54 milliequivalents. The balances, however, were not significantly different.

The sodium excretion for the following days continued to stay higher in the patients in group 2 than in group 1, but the difference is statistically significant only on the

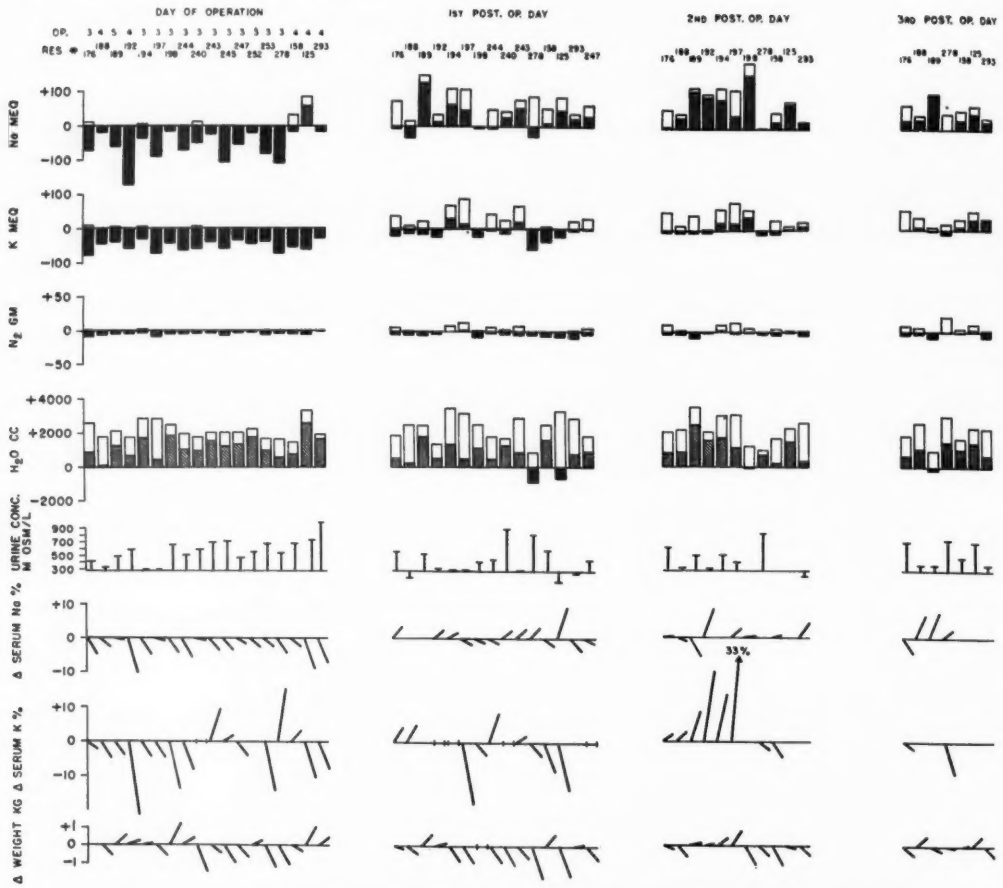

FIG. 1. Group 1, 18 control patients, on the day of operation received dextrose in water, only. From the first to the third postoperative days, the patients were mostly on oral intake. The patients are identified by the unit number in the top of the figure. The severity of the trauma is estimated as explained in the text and shown above the patient's unit number on the day of operation. The columns represent the intakes, outputs, and resulting balances (positive balance crosshatched; negative balance black) for sodium, potassium, nitrogen, and water. The lines represent the urine osmolality, the percentage change in serum sodium and potassium, and changes in body weight, all over 24 hour periods.

second postoperative day. The same is true regarding the difference in sodium balance.

In Figures 1 and 2, the sodium, potassium, nitrogen, and water balances are shown as suggested by Moore and Ball, that is, the intake is plotted from zero and up; the output from the top of the intake column down. Positive balance is crosshatched above zero and negative balance is black below zero.

The urine concentration is plotted as milliosmols per liter, the baseline being 280 milliosmols per liter which is taken as average normal serum osmolality.

The serum sodium and potassium concentrations are presented as percentage changes over a 24 hour period and the weight changes, in grams over the same 24 hour period.

The severity of the trauma is roughly

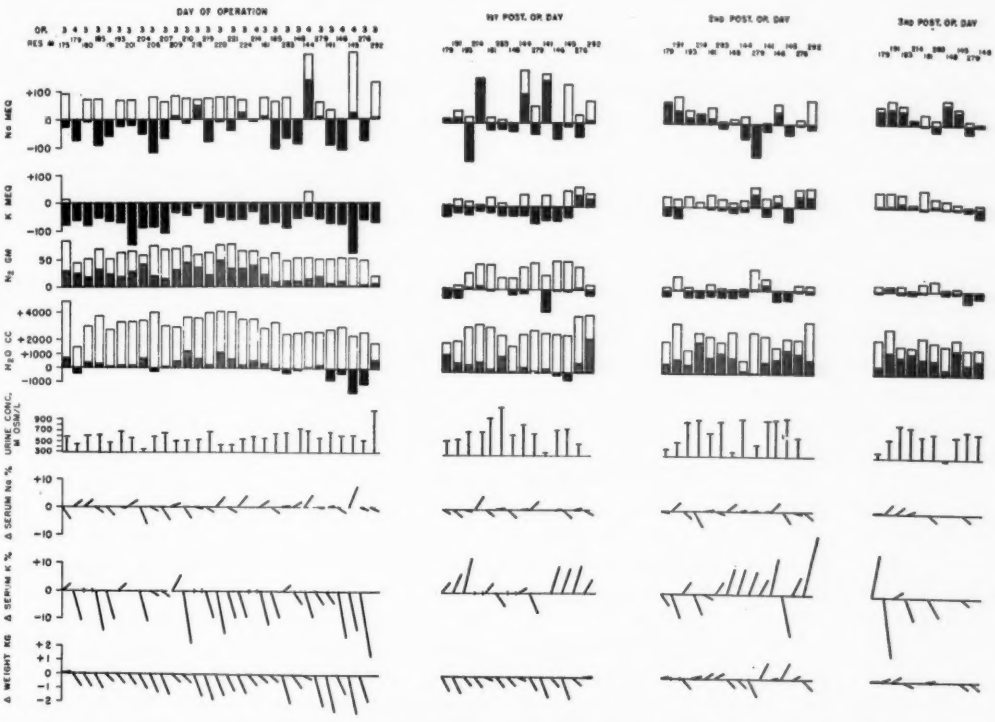

FIG. 2. Group 2, 29 patients all received urea on the day of operation. The majority also received urea on the first postoperative day. On the second and third postoperative days, the patients were on oral intake. The patients are identified by the unit number in the top of the figure. The severity of the trauma is estimated as explained in the text and shown above the patient's unit number on the day of operation. The columns represent the intakes, outputs, and resulting balances (positive balance crosshatched; negative balance black) for sodium, potassium, nitrogen, and water. The lines represent the urine osmolality, the percentage change in serum sodium and potassium, and changes in body weight, all over 24 hour periods.

estimated by adapting a scale 1 to 10 as done by Moore and Ball. An uncomplicated prostatectomy is thus estimated to 3, a gastrectomy 4 to 6, and a cholecystectomy with exploration of the common bile duct 4 to 5. This estimation is shown at the top of each figure on the day of operation.

It is possible to follow the individual patient, in Figures 1 and 2, and find trends which might be obscured in the statistical evaluation.

On the day of operation, 5.5 per cent of the patients in group 1 had a positive sodium balance as compared with 28 per cent in the group 2. Only 5 out of 18 patients in group 1, however, were given sodium, while 22 out of 29 patients in group 2 received sodium.

On the first postoperative day, 66 per cent of the patients in group 1 were in a positive sodium balance compared with 42 per cent of group 2. On the second and third postoperative days, the figures were 91 per cent versus 50 per cent, and 100 per cent versus 60 per cent, respectively.

The patients in the control group and the patients in the urea group on zero sodium intake had, on an average, the same sodium excretion on the day of operation. It can be seen, however, that on the first postopera-

tive day, all patients in group 2 were in negative or close to zero sodium balance, except patients 214, 144, and 141.

Patient 214 was a 62 year old white male who had a chronic pyelonephritis of 8 years' duration. The patient was hypertensive with a blood pressure of 230/70 and he was uremic with a blood urea nitrogen of 74 milligrams per cent, when he was operated upon. A left nephrectomy and cystolithotomy were performed, and the operation as well as the postoperative course was uncomplicated.

Patient 141 was a 67 year old white female with an arteriosclerotic heart disease for which she was treated with a low sodium diet and digitoxin. She had rheumatoid arthritis of 10 years' duration for which she had received cortisone for 5 years. She was admitted for cholelithiasis. Preoperatively, she was placed on a low sodium diet and her cortisone dose was adjusted. The patient was subjected to a cholecystectomy which was difficult but uncomplicated, as was the postoperative course.

These 2 patients thus had good reasons for sodium retention prior to surgery. On the other hand, the decrease in renal function did not prevent a good response to the urea load and both patients had a good diuresis with the expected weight loss. On the second postoperative day, when urea was not given, both patients retained water and gained weight.

The third patient (No. 144) was a 62 year old white female with normal kidney function prior to surgery, who had an exploratory laparotomy with lysis of adhesions. The operation was uncomplicated except for a drop in blood pressure with 120/80 to 80/55, lasting for 1 hour. This patient had some sodium retention on the first postoperative day, but her actual sodium excretion was of the same magnitude as the average for the patients in this group, and on the second postoperative day she was in a negative balance. She had no water retention and a slight increase in serum sodium concentration.

The potassium balance for the patients as a whole was negative on the day of operation and mostly so on the first postoperative day. The potassium excretion was higher in the urea group, but without any apparent relation to the excretion of sodium. The potassium balance in some of the patients became zero while there still was sodium retention present. The serum potassium concentration decreased in patients in both groups on the day of operation, but returned to normal values again in the immediate postoperative period. It was stated in a previous article (6) that the serum potassium did not change following surgery when 4 per cent urea was given, but this observation did not seem to hold true in a larger series of cases.

The large positive nitrogen balance in group 2 was due to the administration of urea. Calculated on the basis of intake and output of nitrogen with the increase in blood urea nitrogen subtracted, the nitrogen balance from metabolism was equally negative in the patients in the two groups. The incomplete return of the urea load in several cases (Nos. 204, 210, 218, 220, 214) was thought to be a reflection of a somewhat decreased kidney function, even though this did not result in a decreased water return or a different way of handling the electrolytes. In the later postoperative period, the patients in both groups went into zero or almost zero nitrogen balance.

DISCUSSION

The results of this study appear to indicate that sodium excretion in postoperative patients is slightly higher when diuresis has been promoted by administration of a 4 per cent urea solution and that the commonly described postoperative sodium retention is thus prevented.

LeQuesne and Lewis reported an invariable sodium retention of about 100 milliequivalents on an intake of 170 milliequivalents of sodium on the day of operation and a continuous fall in urine sodium excretion to a minimum on the fourth day,

while our patients receiving urea had, on the average, a higher sodium excretion despite a lower intake.

It might be expected that sodium retention without water retention would result in an increase in serum sodium concentration while sodium as well as water retention could maintain or lower the concentration. The patients in the control group, receiving 5 per cent dextrose in water, only, gained weight and their serum electrolytes became diluted. This is a common postoperative pattern and parallels the cases described by LeQuesne and Lewis in which the weight gain was found to be due to water retention.

The dilution of electrolytes, especially sodium, has been explained by some as a result of transfer of sodium from the extracellular to the intracellular space in exchange for potassium. In most patients receiving urea, however, no serum sodium dilution takes place. It appears then that the best explanation for the commonly observed decrease in serum sodium postoperatively, as in our control group, is dilution secondary to water retention.

The steady decrease in sodium excretion in the postoperative period in patients in both groups is more pronounced in the control group. The difference, however, appears quantitative rather than qualitative.

It has been suggested that a decrease in serum sodium concentration, as such, will provoke sodium retention in the postoperative period (5). This theory was substantiated by the fact that the patients in the control group had an increasing positive sodium balance on the first and second postoperative days, following a drop in serum sodium on the day of operation. No such retention was present in the patients in the urea group on the same 2 days. Clearest was the difference on the second postoperative day, when no urea was given to any of the patients in either group. On this day, the patients in the control group excreted less sodium than the patients in the urea group, in spite of the former having had a sodium intake almost doubly high.

Seldin and Tarail found that, while glucose and mannitol augment sodium excretion, urea excreted in comparable amounts produces only minor changes in sodium excretion. Urea-induced osmotic diuresis, as such, does not prevent all types of sodium retention. Administration of a 4 per cent urea solution, however, prevents water retention and, indirectly, postoperative sodium retention by maintaining homeostasis in regard to water. When other factors such as renal damage (Nos. 214, 144) or cortisone administration (No. 141) are present, the patients still have sodium retention, in spite of unchanged serum sodium and a good urine output.

Llaurado and Woodruff (2) found a linear relationship between the aldosterone activity of the urine and the logarithm of the sodium-potassium ratio of the patients' urine before and after operation. By the time this ratio returns to its preoperative level, the aldosterone level also has returned to preoperative level. Zimmermann likewise found an increase in aldosterone activity in the postoperative period. Llaurado and Woodruff (3) state that the postoperative elevation of aldosterone activity may occur at any stage of the first 24 hours postoperatively, but they found no correlation between the magnitude of the change in serum sodium and potassium, on the one hand, and the extent or the time of aldosterone increase, on the other. The sodium retention found in our patients, however, seems to indicate some interdependence between serum sodium concentration and sodium retention.

The question remains whether the postoperative sodium retention is due to a decreased filtration in the kidneys, secondary perhaps to the decrease in serum sodium, or whether it is due to increased tubular reabsorption resulting from increased hormonal activity, or, perhaps unrelated to either. The presented data do not answer this question, but it might be of interest to determine the aldosterone production postoperatively. An increased aldosterone production in the patients in group 1, who

received 5 per cent dextrose in water only, could be secondary to the described decrease in serum sodium. If, however, aldosterone production is also increased in the patients in group 2, who received urea, such an increase must be a result of the trauma, since serum sodium is generally unchanged in these patients.

It is emphasized that other types of sodium retention, such as seen in patients with renal damage or on steroid therapy, are not prevented by the administration of 4 per cent urea. Whatever the role of aldosterone is, it appears that the postoperative sodium retention found in the patients in the control group is at least in part secondary to the posttraumatic antidiuresis. The urinary sodium concentration does not differ significantly in the patients in the two groups, so the lack of sodium retention in the urea group appears to be due to the higher urine volumes. This means that postoperative sodium retention can be avoided in the average case, if a daily urine volume of 2 to 3 liters is obtained by the administration of 4 per cent urea. Such a regimen will also prevent water retention and consequent serum dilution, in short, will maintain homeostasis in regard to sodium and water.

SUMMARY

Two groups of patients were studied: group 1 (control group) 18 patients who in the postoperative period were given 2,000 to 3,000 cubic centimeters of 5 per cent dextrose in water; group 2 (urea group) 29 patients who in part of the postoperative period were given about 3,000 cubic centimeters of 5 per cent dextrose in water with 4 per cent urea and 80 milliequivalents of sodium chloride. Balance studies were carried out for the day of operation and 3 postoperative days.

While dilution of serum sodium took place in the patients in group 1, homeostasis in regard to water and sodium was maintained in the patients in group 2. There appeared to be no exchange of extracellular sodium ions with intracellular potassium ions in the patients who were treated with urea.

Sodium excretion was slightly higher in the patients in the urea group, and no sodium retention was present except in 3 patients, of whom 2 had decreased renal function and the third was on cortisone treatment.

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THE EFFECTS OF TEMPORARY ARTERIAL, VENOUS, AND ARTERIOVENOUS OCCLUSION UPON INTESTINAL BLOOD FLOW

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ACCURACY in measuring intestinal blood flow has been difficult to achieve in the past; however, the method recently described by Neely and Turner (2) enables intermittent determination of blood flow in intestinal segments. This method may be readily adapted to determining the effects of injected substances upon intestinal circulation. The effects of temporary arterial or venous occlusion upon segments of the ileum, as measured by this method, are reported herein. These effects must be evaluated if we are to understand better the underlying mechanisms of certain gangrene-producing conditions of the bowel.

The blood flow procedure used in this study has certain advantages over previous methods. First, the method requires relatively simple preparation. Second, the administration of anticoagulants, which have been shown by Crowell and associates to influence vascular reactivity, is not required.

METHODS

Adult mongrel dogs were anesthetized with nembutal and a midline abdominal incision was made. A segment of the ileum was selected equidistant from the ligament of Treitz and the cecum. The artery and vein to this segment were dissected from the enveloping mesentery, and the segment was denervated as far as was surgically feasible. The blood vessels were sprayed with novocain during the dissection to prevent spasm. The bowel segment was then cut from the remainder of the ileum by dividing at a point midway of the arcade on each side of the vessel pair. All bleeders in the severed ends of the isolated segments were ligated at this time. The lumen was allowed to remain patent in order to prevent fluid accumulation in the segment. The preparation was, in effect, an isolated segment of small intestine with no connection to the animal except its vascular pedicle. The isolated segment was positioned on an aluminum plate suspended from a Statham Model G-1-8-350 displacement transducer. The height of the transducer was such that the artery and vein were held in horizontal position. The transducer and a continuous recorder system were calibrated in terms of grams. The intestinal segment was weighed by zero suppression of the recorder before and after the occlusion periods. With the recorder running, the vein was suddenly occluded. Change in weight of the organ was recorded graphically upon a suitable time base. Change in weight with time was proportional to blood flow.

After control measurements of blood flow had been obtained, the artery, vein, or both were clamped for various lengths of time. In one group the vein was clamped for 30 minutes; flow was measured immediately after, 1 hour after, and, occasionally, 2 hours after release of the clamped vein. In other dogs the arteries of the bowel segments were clamped for 1 hour and the rate of flow was measured immediately, and at 1 hour and 2 hour intervals after releasing the artery. In

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TABLE I.—BLOOD FLOW (C.C. PER GRAM PER MINUTE) IN INTESTINAL SEGMENT BEFORE AND AFTER 30 MINUTE VENOUS OCCLUSION

Dog No.	*Control*	*Immediately after release*	*One hour after release*
4- 3-2	0.36	0.14	0.21
5- 1-2	0.24	0.00	0.06
5- 1-1	0.16	0.11	0.20
5- 2-1	0.21	0.19	0.15
5- 2-2	0.46	0.00	0.17
6- 3-1	0.22	0.08	0.14
7-14-2	0.19	0.00	0.06
7-14-3	0.39	0.04	0.07
7-14-4	0.21	0.08	0.07
Mean	0.27	0.07	0.13
		(P<.005)	(P<.005)

another group both the artery and the vein of the intestinal segment were clamped and measurements of blood flow made as described. The nature of the experimental procedure required the anesthetized animal to remain in the same position for periods ranging up to 3 hours. In a group of 10 animals the rate of blood flow was determined as described in the experiments mentioned except that the blood vessels were not clamped. No significant change in blood flow occurred over a 3 hour period. Therefore, it may be assumed that significant alterations in the rate of blood flow in the intestinal segments are due to the period of vascular occlusion.

To determine whether the bowel would survive after longer periods of occlusion, the following study was done. The blood supply of the terminal ileum of certain dogs was isolated and clamped. Rubber bands were placed about the bowel above and below the segment in question to insure that no cross-circulation could occur. In one series of animals the artery and vein were occluded for 4 hours. After the occlusion period the rubber bands were removed from the intestine and the abdomen was closed. The animals were returned to their cages and their survival times determined. In another series the mesenteric vein draining the segment was occluded for 4 hours, but the artery remained patent. The vein was then released and survival time observed as described.

TABLE II.—BLOOD FLOW (C.C. PER GRAM PER MINUTE) IN INTESTINAL SEGMENT BEFORE AND AFTER 1 HOUR OCCLUSION OF ARTERY AND VEIN

Dog No.	*Control*	*Immediately after release*	*One hour after release*
4-23-1	0.14	0.00	0.14
4-24-1	0.17	0.18	0.00
5-22-1	0.33	0.28	0.26
5-15-1	0.38	0.17	0.20
5-21-1	0.19	0.19	0.00
6- 4-1	0.10	0.21	0.24
6- 6-1	0.18	0.18	0.17
7-23-1	0.15	0.15	0.12
7-23-3	0.25	0.41	0.29
7-23-4	0.66	0.88	0.28
Mean	.255	.265	.170
		(P<.80)	(P<.10)

RESULTS

The mean control blood flow in the 29 dogs studied was found to be 0.31 cubic centimeter of blood per gram of gut tissue per minute.

Thirty-minute occlusion of bowel segment vein. This series consisted of 9 dogs in which the venous drainage from the isolated ileal segment was occluded for 30 minutes. The artery was allowed to remain patent. Blood flow data are given in Table I. The reduction in blood flow 5 minutes after release of occluding clamps was statistically significant (P value of .005). Blood flow remained significantly decreased 1 hour after release of occlusion (P value of .005).

One hour occlusion of artery and vein. In 10 animals the artery and vein from the isolated ileal segments were occluded for 1 hour. Blood flow data are presented in Table II. No statistically significant changes in blood flow were observed in this group.

One hour occlusion of bowel segment artery. In 10 animals the arterial supply to the isolated ileal segment was occluded for 1 hour. Blood flow data are presented in Table III. A significant (P value .01) reduction in blood flow occurred 5 minutes after release of the occluding clamps. Blood flow was still significantly decreased (P value .01) 1 hour after the occlusion.

Occlusion of intestinal artery or vein for 4 hours. In 6 animals the artery supplying the isolated ileal segment was occluded for 4 hours. In 6 other animals the vein draining the segment was occluded for 4 hours while the artery remained patent. The results are

shown in Tables IV and V. It is evident from these data that venous occlusion is more detrimental than arterial occlusion.

DISCUSSION

Reactive hyperemia after circulatory insults such as hypoxia and short term vascular occlusion is a well known phenomenon. However, following the long term circulatory occlusions in this study, hyperemia was not observed in the intestinal segments. The hyperemic response has also been reported by Neely and Turner (3) to be absent in the kidney after this organ was subject to prolonged circulatory stasis. The significance of this finding is not clear at the present time.

This study demonstrates that a venous occlusion of the intestine is considerably more detrimental than an arterial or arteriovenous occlusion. After a 30 minute stasis of the mesenteric vein of the intestinal segment, blood flow was reduced to very low levels. In all but 1 case the blood flow was still markedly decreased 1 hour after the occluding clamp was removed. The reason for this great decrease in blood flow after prolonged venous occlusion is not entirely clear. The increased hydrostatic pressure due to the patent mesenteric artery causes increased capillary pressure and exudation of large amounts of fluid into the interstitial space. This reaction results in increased tissue pressure which apparently remains high for a long period of time after the vein is allowed to drain. The diminished blood flow may be a direct result of the mechanical effect of high tissue pressure on the small blood vessels. This phenomenon may also account for the absence of hyperemia following prolonged circulatory stasis. However, it may be noted that the hyperemic response was absent following prolonged arteriovenous occlusion and after occlusion of the artery alone.

The intestine appears to have great tolerance for arterial occlusion. This impression is supported by both the blood flow data and the survival studies after a 4 hour period of arterial stasis. Simultaneous occlusion of the renal artery and vein for 1 hour periods has been shown to be detrimental to renal blood flow after the stasis period (3). In contrast, simultaneous occlusion of the artery and vein of intestinal segments caused no significant change in blood flow. Perhaps the intestine, being a more primitive tissue, can tolerate vascular insults to a greater extent than the kidney. It should also be noted that the oxygen consumption of intestinal tissue per gram is much less than that of renal tissue as Spector has indicated. Throughout the occlusion period peristaltic movements were observed in the intestine. At the end of an hour's arterial occlusion the bowel appeared pale. Upon release of the occluding clamps, however, the intestine immediately flushed and appeared normal.

TABLE III.—BLOOD FLOW (C.C. PER GRAM PER MINUTE) IN INTESTINAL SEGMENT BEFORE AND AFTER ARTERIAL OCCLUSION FOR 1 HOUR

Dog No.	*Control*	*Immediately after release*	*One hour after release*
7-11-1	0.22	0.17	0.20
7-11-2	0.12	0.05	0.05
7-14-1	0.38	0.25	0.26
7-21-1	0.65	0.25	0.38
7-21-2	0.52	0.17	0.30
7-21-3	0.73	0.36	0.16
7-21-4	0.20	0.13	0.12
7-22-1	0.20	0.25	0.22
7-22-2	0.47	0.37	0.40
7-22-3	0.40	0.09	0.11
Mean	0.389	0.209 ($P<.01$)	0.220 ($P<.01$)

TABLE IV.—OCCLUSION OF MESENTERIC ARTERY FOR 4 HOURS

Dog No.	*Died*	*Gut gangrenous*
144	No*	No
123	No	No
178	No	No
24-1	1st day	Yes
24-2	1st day	No
22-1	No	No

*Under "Died" "No" means alive at 10 days when the dogs were sacrificed and gut examined for gangrene.

TABLE V.—OCCLUSION OF MESENTERIC VEIN FOR 4 HOURS

Dog No.	*Died*	*Gut gangrenous*
22-1	3rd day	Yes
24-2	1st day	Yes
26-2	2nd day	Yes
20-2	No	No (killed 14 days)
18-1	No	Wound dehisced; killed; gangrenous gut
18-2	10th day	No

It would be of interest to study the effect of prolonged circulatory stasis on blood flow in organs in the heparinized animal since it has been shown by Crowell that heparin prolongs the survival time in dogs after temporary circulatory arrest.

SUMMARY AND CONCLUSIONS

1. The mean control blood flow in 29 intestinal segments was found to be 0.31 cubic centimeter per gram of tissue per minute.

2. Thirty-minute occlusion of the venous drainage of intestinal segments results in a significantly decreased rate of blood flow even 1 hour after restoration of flow.

3. A significant but much less marked decrease in blood flow through the intestinal segments occurred following 1 hour's occlusion of the artery.

4. No significant alteration was found in the rate of blood flow in the intestinal segments after arteriovenous stasis was maintained for 1 hour.

5. In a short series of dogs the incidence of intestinal gangrene was much higher after 4 hour occlusion of the mesenteric vein than it proved to be after occlusion of the mesenteric artery.

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THE TECHNIQUE OF SYNCHRONOUS (TWO TEAM) ABDOMINOPERINEAL PELVIC EXENTERATION

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THE TERM pelvic exenteration should denote total removal of the pelvic peritoneum, fat, lymph tissue, and upper genitalia, plus the bladder (anterior exenteration) or the rectum (posterior exenteration) or both (total exenteration). It does not apply to radical hysterectomy alone, for instance, or to combined abdominoperineal resection of the rectum even if the genitalia are included in continuity.

Usually, exenteration operations are accomplished via an abdominal approach alone. The tissues are mobilized from above, down as far as the levator ani muscles, and then the urethra, vagina, and rectum are transected at this level. However, when cancer extends low in any of these structures or is primary in the urethra, vulva, vagina, rectum, or anus, it is advisable to do a perineal excision in continuity as well. While this can be done to a certain degree from above, we prefer a separate perineal approach.

Earlier, we performed combined abdominoperineal exenterations with one surgical team, first completing the abdominal part with the patient supine and then the perineal part with the patient in lithotomy position. But our experiences with synchronous (two team) abdominoperineal resection of the rectum encouraged us to apply this technique in pelvic exenteration.

As our experience with the two team technique increased, perineal excision was considered a necessary part of almost every exenteration whether partial or total. It is easily accomplished by two teams without additional time and gives more adequate tumor clearance, at least in some cases which cannot always be properly appraised except by the pathologist after the specimen has been obtained.

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LITERATURE

Little has been written concerning two team abdominoperineal operations, and the articles that are available deal almost exclusively with the application of the technique to resection of the rectum. However, Canonico has employed it for pelvic exenteration (4, 5), and Howkins has applied it to radical hysterectomy. In September 1957, before a meeting of the American Association of Obstetricians and Gynecologists at Hot Springs, Virginia, Howkins presented a motion picture illustrating his technique for this operation.

RATIONALE OF TWO TEAM OPERATION

Pelvic exenterations are formidable operations plagued by numerous serious complications which often lead to prolonged hospitalization. They take from 3 to 9 hours to complete; the mortality rate varies from 4 to 33 per cent, and the 5 year salvage rate is reported to be 7 to 25 per cent (Table I). Obviously, there is much room for improvement.

Comparison of one and two team operations for cancer of the rectum showed that the two team approach saved significant operating time, was not more shocking, gave a smoother operative course, and led to a lessened mortality (12). Morton reported in addition a marked improvement in 5 year survival rates. With two teams the removal of bulky tumors is greatly facili-

TABLE I.—SURVEY OF THE LITERATURE

Authors	*Year*	*No. of cases*	*Operation time, hrs.*	*Mortality rate, per cent*	*5 yr. survival rate, per cent*
Bricker	1951(1)	32	5 to 7	34	
Bricker	1954(2)	118	4 to 8	8 to 19	23
Brunschwig	1954	315		26.6	12
Douglas	1957	23	4.5 to 9.6	4.3	20
Parsons	1955	116		23 to 33	25
Schmitz	1957(11)	51		33.3	11
Wawro	1957	44		9	7

tated, and hemostasis can be more easily and more adequately attained.

POSITIONING THE PATIENT

No special tables, rests, or leg stirrups are used. The patient is put to sleep in the supine position. Inhalation anesthesia has been administered in all cases but spinal anesthesia would not alter the technique.

Once asleep, the patient is placed in the lithotomy position with the thighs flexed 45 to 60 degrees at the hips, and the legs flexed 80 to 90 degrees at the knees, with the extremities widely apart and the pelvis elevated off the table by a sandbag or folded blanket under the sacrum. Then the table is tilted 10 to 20 degrees into the Trendelenburg position and a large instrument table is placed over the head end, respecting the anesthesiologist's room as much as possible. The skin is prepared by soap and water scrub followed by a mercurial antiseptic. The bladder is emptied by catheter. The patient is covered with sterile half sheets in such a manner that the abdominal and perineal fields are continuous.

There is sufficient room for an abdominal team of two or three surgeons and an instrument nurse, and a perineal team of two surgeons and an instrument nurse.

TECHNIQUE OF TOTAL EXENTERATION

Abdominal dissection. The following steps are used in performing an abdominal dissection:

1. A lower midline or left paramedian incision is made from the symphysis pubis to 3 inches or so above the umbilicus (Fig. 1 inset). A transverse incision would interfere with the placement of the ileal and sigmoidal stomas.

2. The supracolic compartment of the peritoneal cavity is explored, particularly the liver; the kidneys are palpated for hydronephrosis; the infracolic compartment is explored, particularly the periaortic nodes.

3. The local pelvic situation is appraised as to operability which may entail opening the previsical and obturator spaces.

4. If the pelvic lesion seems resectable for cure, the pelvic peritoneum is incised on the right side by grasping and dividing the ovarian ligament and its vessels. The opening is extended upward along the common iliac vessels to the aortic bifurcation and downward to the external inguinal ring, and then anteromedially into the prevesical space to meet the abdominal incision.

5. The dissection of the right pelvic lymph nodes is carried out along the common iliac vessels, downward along the external iliac vessels, around and behind the hypogastric vessels and into the obturator fossa, sparing the obturator nerve but taking the obturator vessels. During this dissection the ureter is carefully displaced medially leaving it temporarily attached to the peritoneum. As the hypogastric artery is encountered it is tied in continuity close to the external iliac artery. The hypogastric vein is spared until later to minimize "back-bleeding" for the perineal team (Fig. 1).

6. Steps 4 and 5 are repeated on the left side.

(As soon as both hypogastric arteries are tied and the delicate lymph node dissection is nearly completed, the perineal team begins to work.)

7. The ureters are divided as low as the disease process permits and the proximal ends are tied to allow them to dilate with urine. The ureters are dissected upward 5 to 7 centimeters along with a flap of peritoneum and adventitial tissue to preserve their vascular supply (Fig. 1).

8. The superior hemorrhoidal vessels are isolated, divided, and tied close to the root of the mesosigmoid. The sigmoid mesentery

is divided from this point outward to the place on the sigmoid arch selected for colostomy.

(By this time the perineal team has completed steps 1 through 5 of their dissection and from this point on the two teams work in conjunction.)

Perineal dissection. This dissection is performed by the following steps:

1. A purse-string suture of silk is placed about the anus and another about the vaginal orifice (Fig. 2 inset).

2. Elliptic incisions are made from just above the clitoris anteriorly, around the vulva and anus to the tip of the coccyx posteriorly (Fig. 2 inset).

3. The incisions are developed inward to the symphysis pubis, along the rami to the ischial tuberosities and to the coccyx. In so doing the ischiocavernous and transverse perineal muscles are transected far laterally. During the dissection bleeding is usually minimal but the inferior hemorrhoidal and other branches of the pudendal vessels may ooze a little and are tied.

4. The plane of incision is carried upward along the inner surface of the ischium to the lateral attachments of the levators. This muscle is cleared along these attachments from front to back (Fig. 2).

5. By sharp dissection the anococcygeal ligament is divided posteriorly and the urogenital fascia anteriorly. Then a finger can be passed through above the levator ani muscle so that it is easily divided in segments with a scissors immediately against its lateral attachments (Fig. 2). This is done on both sides.

(About this time, the abdominal team has finished step 8 of their part.)

Combined dissection. Following are the steps taken to perform the combined dissection:

1. The two teams work in unison to mobilize the bladder and urethra from the pubis and lateral attachments by blunt and sharp dissection.

2. The rectum is separated from the sacrum in a similar manner, carefully avoiding the middle sacral vein.

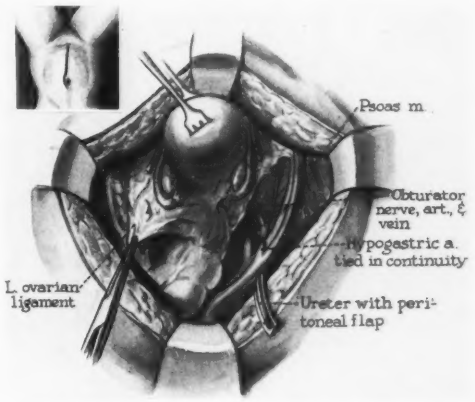

FIG. 1. Abdominal dissection: mobilization of lymphatic tissues completed on right side; about to be started on left side.

3. The lateral lymphatic "webs" are divided on each side. Often the perineal team can readily see and clamp the various branches and tributaries of the hypogastric vessels in the webs which the abdominal team cannot easily see from above until they have been cut or injured (Fig. 3). As this dissection is completed the hypogastric vein and artery are clamped and divided. The various vessels which have been clamped

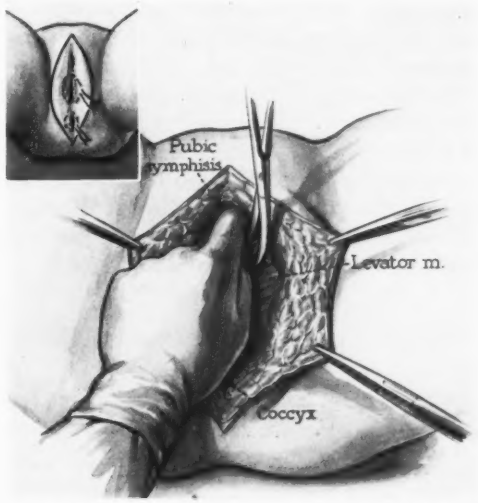

FIG. 2. Perineal dissection: transection of levator about to begin.

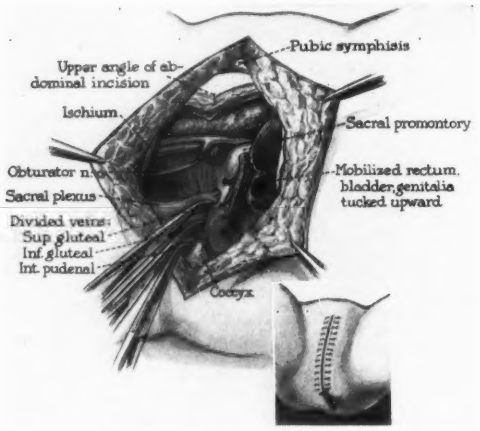

FIG. 3. Combined dissection: angled view through perineal wound showing completed mobilization of right lymphatic web. The vessels have been clamped from below but will be ligated from above.

by the perineal team, because of better visibility, are then tied from above by the abdominal team, because the anatomy permits this much more easily. The perineal team helps in passing the sutures about the clamps and vessels.

4. The entire specimen is then passed upward and out through the abdominal wound. The sigmoid is divided between DeMartel blades at the point selected for colostomy; the proximal end is covered with gauze and laid on the anterior abdominal wall.

Reconstruction. This procedure is carried out in the following manner:

1. If necessary for hemostasis, the pelvis is packed by the abdominal team, and the ends of the pack are brought out through the perineal wound. If the pelvis is dry, no packing is done; but a "bundle" of 4 Penrose cigarette drains is placed in the hollow of the sacrum and brought out through the perineal wound.

2. A "lid" is placed over the pelvic funnel, whether it is packed or not, to prevent prolapse of the small bowel into it. (The incidence of small bowel obstruction after exenteration is significantly high.) This "lid" of steel or tantalum mesh is sewed to the anterior abdominal wall, the iliopsoas muscles, and the retroperitoneal tissues near the sacral promontory. Care is taken to avoid pressure where the mesh crosses the iliac vessels (Fig. 4).

3. Urinary diversion is carried out. We now prefer the Bricker ileal conduit after total exenteration. The ileocutaneous anastomosis is made in the right lower quadrant of the abdominal wall after excising a button of flesh from the skin, fascia, and peritoneum to match the caliber of the ileum.

4. The colostomy is established in the left lower quadrant of the abdominal wall by the flush mucosa-to-skin technique after excising an appropriate button of flesh from the wall, as for the ileum.

5. The abdominal incision is closed without drainage.

TABLE II.—TYPES OF PELVIC EXENTERATIONS

	One team	*Two team*	*Totals*
Abdominal approach	33	0	33
Anterior	12	0	12
Posterior	9	0	9
Total	12	0	12
Abdominoperineal approach	8	27	35
Anterior	3	7	10
Posterior	3	5	8
Total	2	15	17
Grand total	41	27	68

TECHNIQUE OF ANTERIOR EXENTERATION

The steps are essentially the same as for total exenteration, except that the rectum and anus are spared by bringing the posterior plane of dissection through the pouch of Douglas and the rectovaginal septum.

If the preoperative intravenous pyelograms show normal structure and prompt function bilaterally, the urinary stream may be safely diverted by ureterosigmoidostomy, since about 50 per cent will be satisfactory on a long term basis. If hydronephrosis, ascending infection, or electrolyte problems arise later (even after years) a Bricker conduit may still be constructed.

If the preoperative studies show the urinary tract to be below par, a Bricker ileal conduit is constructed at the end of the anterior exenteration.

TECHNIQUE OF POSTERIOR EXENTERATION

Again, the steps are much the same as for total exenteration, but the anterior plane of dissection is carried through the vesicogenital cul-de-sac and the vesicovaginal septum, thus sparing the bladder and ureters.

No urinary diversion is necessary and the proximal end of the transected sigmoid is established as a colostomy in the left lower quadrant of the abdominal wall.

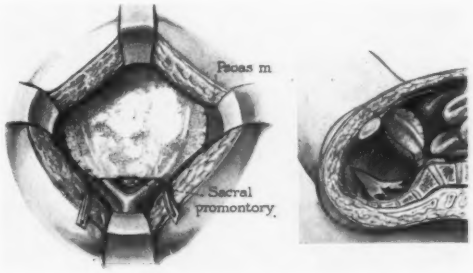

FIG. 4. Reconstruction: the pelvic "lid."

MATERIAL

To date, we have performed 68 pelvic exenterations (Table II). In 33, no perineal dissection was done; in 35 a combined abdominal and perineal dissection was done. Of these 35 cases, in 8 of the earlier ones the operation was done by one team, but in the other 27 the operation was done synchronously by two teams.

The sites of the primary disease for which the one and two team operations were done are quite similar (Table III), and it is obvious that in the vast majority the indication is carcinoma of the cervix.

It is interesting that to date we have treated the cervix cancers about equally by anterior, posterior, and total exenteration (Table IV).

DISCUSSION AND COMMENT

Obviously, the foregoing descriptions are standardized and simplified. They represent the "routine" or desirable plan of operation, but many variations and improvisations are necessary as unusual problems or situations are encountered during the progress of the exenteration. These adjustments seem to be more easily made with two teams because the number of possible variations in approach is increased.

It is early and the series of cases is small for comparison of the one team and two team exenterations. It is our impression, however, that we are saving time and blood by the two team technique and that the postoperative course is smoother, and the mortality rate less.

In general, lower urinary tract cancer is most apt to be suitable for anterior exenteration and rectal cancer for posterior exenteration. We are tending away from anterior and posterior exenterations for genital cancer, in favor of the total operation, especially in carcinoma of the cervix. Too often dissecting through the rectovaginal or vesicovaginal septum that has been irradiated leads to fistula formation. More importantly, however, the distance of clearance from the tumor is apt to be inadequate, and the lymphatics around the cervix are such that recurrence is common in the rectum or bladder that has been left. Actually, the total operation is just as easy, or easier, than the partial extirpation and often

TABLE III.—SITE OF PRIMARY DISEASE

Site of 1° disease	*One team operation*	*Two team operation*	*Totals*
Urethra	2	0	2
Bladder	2	1	3
Vulva	0	1	1
Vagina	1	1	2
Cervix	30	21	51
Corpus	3	0	3
Ovary	2	1	3
Rectosigmoid	1	2	3
Totals	41	27	68

TABLE IV.—SITE OF DISEASE AND TYPE OF OPERATION

Site of 1° disease	*Ant. ex.*	*Post. ex.*	*Total ex.*	*Total*
Urethra	2	—	—	2
Bladder	3	—	—	3
Vulva	—	—	1	1
Vagina	1	—	1	2
Cervix	15	12	24	51
Corpus	1	1	1	3
Ovary	—	2	1	3
Rectosigmoid	—	2	1	3
Totals	22	17	29	68

shorter and less traumatic. As much as one would like to preserve a natural fecal or urinary reservoir one must also remember that exenteration is a "last ditch stand" against cancer and that the operation must be an adequate one. We mentioned earlier at least a theoretic value for including perineal excision in almost all exenterations.

Our intention is to continue the two team synchronous abdominoperineal exenteration until we have evidence that this attack is, or is not, superior to those more commonly in use.

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TRANSFORMATION OF A LOW GRADE PAPILLARY CARCINOMA OF THE THYROID TO AN ANAPLASTIC CARCINOMA AFTER TREATMENT WITH RADIOIODINE

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IT HAS BEEN SHOWN by Furth, Foulds, Bielschowsky, Purves, and others that in laboratory animals the stimulation of target organs by trophic hormones causes first hyperplasia, then nodular change, then the development of cancers that are dependent for their growth on the persistence of the imbalance that caused them. Finally, if the endocrine imbalance persists, undifferentiated cancers that are autonomous and unresponsive to endocrine control may be produced. An example is the induction in rats of autonomous, undifferentiated cancer of the thyroid following prolonged suppression of the output of thyroid hormone by administration of thiouracil.

In man, Maloof and associates, Thomas, and Crile present evidence that suggests that many differentiated cancers of the thyroid are "endocrine dependent." Not only is the rate of growth of these cancers increased by any treatment that induces hypothyroidism and increases the output of thyroid-stimulating hormone (TSH), but also, just as in animals, prolonged stimulation by TSH may convert a low grade, differentiated, and endocrine-dependent tumor into a highly malignant anaplastic cancer that is no longer dependent on TSH. Seven cases in which this transformation has taken place have been collected in a previous report (2), and since that report Frazell and Foote have reported 6 others.

The following report is of a similar case in which, following a period of myxedema induced by treatment with radioiodine (I^{131}), a cervical metastasis of a low grade and probably dependent papillary carcinoma was converted to a highly malignant, undifferentiated, and autonomous cancer.

The patient was first examined at the Cleveland Clinic in 1925 when she was 22 years old. She gave a history of 2 nodules having developed in the left side of her neck 6 years before. They had enlarged slowly and were easily visible and palpable. They were thought to be tuberculous nodes, but no biopsy was done. A roentgenogram of the chest showed calcification at the hilus, and extensive "fibrous" infiltrations over the lower two thirds of the lung. These changes, which now are known to be characteristic of metastatic papillary carcinoma of the thyroid, were interpreted as being the result of tuberculosis. She was given 4 roentgen-ray treatments to the cervical nodes, 1 month apart, each treatment consisting of 30 per cent of an "erythema dose." There was no change in the size of the nodes.

In June of 1926 the largest of the cervical nodules was removed. It was a well encapsulated, spherical mass 2½ centimeters in diameter with a homogeneous, firm, brownish-yellow cut surface. Sections through the node showed it to be composed of well defined papillary formations and acini filled with colloid. The stalks were covered by several layers of cuboidal epithelial cells. Connective tissue trabeculae separated the acini. The pathologic diagnosis was either a metastasis of a papillary carcinoma of the thyroid or an "aberrant thyroid adenoma."

The patient refused further treatment and was not seen again until 1939. She then had nodules in both thyroid lobes, the larger the

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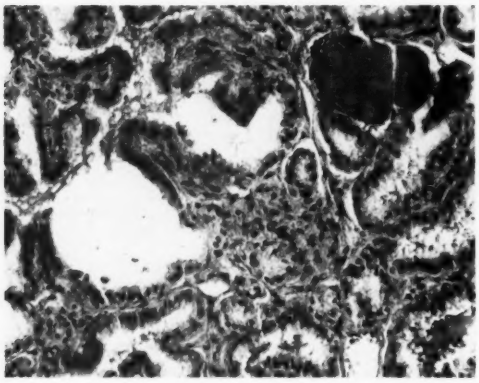

FIG. 1. Appearance of tumor in 1926. Well differentiated follicular variant of a papillary carcinoma, metastatic in cervical lymph node. ×160.

"size of a plum," and smaller nodules in both lateral cervical regions. In the isthmus there was a nodule "the size of a walnut." She felt well, however, and was gaining weight. She again refused operation.

The patient returned in September 1953, 34 years after the nodules were first noticed, because of hoarseness. The left vocal cord was paralyzed. She had nodules in the thyroid gland and lateral cervical region but they were smaller than implied by their description 14 years before. A roentgenogram of the chest showed evidence of diffuse, nodular, metastatic lesions in the base of both lungs. Tracer studies showed that the metastases were concentrating I^{131}.

Between September 1953 and January 1955, a total of 210 millicuries of I^{131} was given in divided doses of 30 millicuries each. Roentgenograms of the chest in April 1955 showed regression of the metastases. The basal metabolic rate fell from minus 12 per cent in September 1953 to minus 24 per cent in October 1954, and to minus 33 per cent in January 1955. Clinically the patient had myxedema. Although the left vocal cord was still paralyzed, the patient's voice returned to normal a few weeks after the first treatment with I^{131}.

In February 1955, the patient was given desiccated thyroid in doses of 2 grains daily, increased to 3 grains daily in April 1955.

In May 1957, roentgenograms of the chest showed no trace of the metastatic lesions in the lungs. The nodules in the lateral lobes of the thyroid and in the lateral cervical regions had disappeared, and only a small round nodule in the isthmus of the thyroid remained. This was thought to be a cystic adenoma.

In November 1957, 35 months after the last treatment with I^{131}, the patient noticed a rapidly growing mass in the right supraclavicular region. Roentgenograms of the chest showed no evidence of metastasis. The patient was advised to have the supraclavicular tumor removed.

In the next month the mass in the right supraclavicular region more than doubled its size, and in January 1958 an attempt was made to remove it. It was fixed, and invaded all surrounding tissues so that it was impossible to remove it completely. The lateral lobes of the thyroid contained no palpable nodules. The midline nodule was removed and proved to be a simple adenoma.

The supraclavicular tumor was a highly anaplastic and undifferentiated carcinoma which bore no resemblance to the tissue of the original biopsy specimen (Figs. 1 and 2). Examinations of the ear, nose and throat, and chest revealed no evidence of a primary tumor.

The patient was given cobalt-60 teletherapy[1] with no apparent effect on the growth of the tumor. A large fungating and invasive local recurrence developed, and she died on April 4, 1958, 39 years after the first nodule was noticed and 5 months after the appearance of the undifferentiated carcinoma.

DISCUSSION

The patient had a proved carcinoma of the thyroid for 34 years before she was treated with I^{131}. During the 30 years before treatment neither the primary cancers nor their metastases had enlarged; in fact, it ap-

[1]The radioactive cobalt used was supplied by Oak Ridge National Laboratory, on authorization of the Isotopes Division, United States Atomic Energy Commission, Oak Ridge, Tennessee.

peared to the patient and her examiners that they had grown smaller. The tumor was a follicular variant of a papillary carcinoma which had metastasized early and widely to cervical nodes and lungs. After the years of steady growth the tumor ceased growing, perhaps because the tumor, which contained much colloid, was able to function autonomously and fabricate enough thyroid hormone to suppress the pituitary's output of TSH. In 1953 the observation of a paralysis of one vocal cord suggested that the tumor's growth had been reactivated, although photographs of the patient, the roentgenographic appearance of the pulmonary metastases, and examination of the neck failed to reveal any signs of growth. It is noteworthy that the hoarseness, which called attention to the vocal cord paralysis, disappeared spontaneously despite the fact that the cord remained paralyzed. It is therefore possible that the hoarseness was not caused by the paralysis, and that the paralysis was not caused by further invasion by the tumor but had been present for many years.

The period of clinical hypothyroidism associated with the I^{131} therapy lasted only 3 months, but during this time it is possible that radioresistant cancer cells in one of the cervical nodes were stimulated by TSH to further malignant change. It is unlikely that the undifferentiated cancer was a new primary tumor, because the vocal cord paralysis was on the side opposite from the node in which the undifferentiated cancer developed, and there was no palpable cancer in the thyroid at the time of the operation. It is also unlikely that the undifferentiated cancer originated in some other organ, for no primary source was found.

The question naturally arises as to whether the small dose of roentgen-ray therapy given 28 years before the I^{131} or the ionizing radiation from the I^{131} could have been related to the development of the undifferentiated cancer. There is evidence that radiotherapy causes instability of the genes, and it is possible that the genetic change in

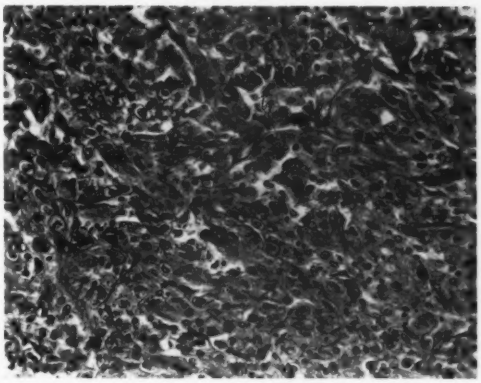

FIG. 2. Appearance of tumor in 1958. Undifferentiated carcinoma invading lateral cervical region. ×160.

the cell was produced by the primary irradiation or by the treatment with I^{131}. If so, it is quite possible that the cancer cells so produced could have lain dormant until stimulated by TSH. In this event, TSH could be considered not the initiating agent but the promoting agent that caused the final growth of the altered cells. An experimental analogy is in the change induced in the skin of animals by carcinogens. Although no clinical cancers may be produced by the original application of a carcinogen, the subsequent painting of the skin with a promoting agent such as croton oil can result in the development of clinical cancers.

The rate of growth of the tumor was such that its size seemed to double in a period of about 1 month. If McWhirter's calculations for the latent period of doubling are correct, and assuming that this cancer was able to double its size each month, it would take 20 months for the cancer to grow from a single cell to a tumor 1 millimeter in diameter, 30 months to make a mass 1 centimeter in diameter, and only 4 or 5 more months to make a tumor the size of the cancer at the time of the second operation (3 centimeters).

It seems likely, in view of these facts, that the change from a differentiated, papillary carcinoma to an undifferentiated, autonomous cancer occurred during the time of exposure to an excess of TSH.

Most tumors that are sufficiently differentiated to take up I^{131} are still dependent on thyroid-stimulating hormone for their continued growth. Most such tumors cease growing or shrink when the output of TSH is suppressed by feeding thyroid. Since treatment of thyroid cancer by thyroid feeding runs no risk of increasing the growth energy of the cancer, it appears that a trial on thyroid should be given before I^{131} is used. Furthermore, if I^{131} is to be used, the period of myxedema should be as short as possible.

SUMMARY

1. A case is reported in which, following a period of myxedema induced by treatment with I^{131}, a low grade papillary carcinoma that had shown no tendency to grow during a period of 34 years was transformed into a highly undifferentiated, rapidly growing, autonomous cancer. This is the fourteenth case of this type to be reported.

2. Experimental and clinical evidence suggests that the increased output of thyroid-stimulating hormone induced by the treatment with I^{131} either initiated the transformation of the cancer to an undifferentiated and autonomous type or promoted the growth of dormant cancer cells.

3. In order to avoid such changes, it is urged that patients with inoperable differentiated thyroid cancers be given a trial of treatment by feeding desiccated thyroid before treatment with I^{131} or roentgen therapy is used.

4. It is also urged that operable papillary carcinomas be removed, even if they are not growing, for it seems possible for some of them to undergo change to a more malignant type.

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AN EXPERIMENTAL STUDY OF SYSTEMIC-CORONARY ANASTOMOSIS

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IN THE PAST FEW YEARS surgeons have directly attacked, with considerable success, the problem of segmental occlusive arterial disease of the distal aorta or major peripheral arteries. The direct surgical approach to occlusive arterial disease has included such procedures as: (1) resection of stenotic or occluded arterial segments with replacement by various types of grafts, (2) bypassing the stenotic or occluded segments with various types of grafts, and (3) thromboendarterectomy of the stenotic or occluded arterial segments. Realizing the magnitude of the problem of the management of arteriosclerotic heart disease, surgeons ultimately commenced to wonder whether the aforementioned surgical procedures would not be applicable to the management of segmental occlusive coronary arterial disease, providing the frequency of occurrence of such disease was significant.

Zoll, Schlesinger, and others (2, 3), in an injection and dissection study of 1,050 human hearts, reported that 50 per cent of patients dying of myocardial infarction have segmental occlusions of the major branch coronary arteries. This same group also noted that approximately 50 per cent of such segmental coronary occlusions occurred within the first 2.5 centimeters of the major branch coronaries. This latter figure jumped to 70 per cent if the first 4 centimeters of each major coronary were included. Furthermore, they reported that most zones of such segmental occlusion are less than 5 millimeters in length.

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It would appear, then, that segmental occlusive coronary artery disease occurs not infrequently. Whether or not such segmental coronary disease is of clinical significance is currently extremely difficult to ascertain and must await more extensive use of coronary angiography as a diagnostic study in large numbers of patients with occlusive coronary artery disease.

Coronary angiography, which has only recently become a valuable adjunct to the diagnostic armamentarium of the cardiologist, has provided a means of establishing the presence of segmental occlusive coronary artery disease. Coronary angiography reportedly reveals not only the presence and extent of segmental occlusive coronary disease but, furthermore, allows an evaluation of the status of the peripheral branches of the major coronary arteries.

Having established that the incidence of segmental occlusive coronary artery disease is more than significant, and having a means of diagnosis, we have, then, a logical rationale for the experimental evaluation of one or more of the previously listed surgical procedures as they apply to the management of segmental occlusive coronary artery disease.

Coronary thromboendarterectomy, although already reported by Bailey as having been applied in the surgical management of segmental occlusive coronary disease in man, seemed to us to require the presence of segmental occlusive coronary disease in the living animal to test its technical feasibility. It would be extremely difficult, if not impossible, to develop segmental occlusive atherosclerotic lesions in canine animals. Therefore, it was our opinion that it would be im-

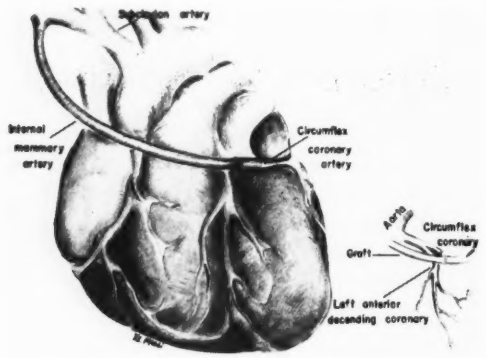

FIG. 1. Systemic-coronary anastomosis utilizing the left internal mammary artery and circumflex coronary artery.

practical to attempt to evaluate coronary thromboendarterectomy.

A systemic-coronary anastomosis, allowing bypass of a segmental stenotic or occluding lesion, does not require the presence of a segmental lesion to allow evaluation of its technical feasibility and clinical applicability. The latter procedure was chosen to evaluate in test animals. It is the purpose of this communication to report an experimental evaluation of systemic-coronary anastomosis in canine animals.

PROCEDURE

Healthy mongrel dogs weighing 16 to 30 kilograms were used in this study. Anesthesia was induced by using intravenous nembutal in a dosage of 30 milligrams per kilogram of body weight. Adequate respiration was maintained by the use of a cuffed endotracheal tube and a respirator utilizing intermittent positive and negative pressure. Continuous electrocardiograms were recorded and monitored during the operative procedure.

In group I there were 14 dogs in which the left internal mammary artery was dissected free from the sixth intercostal space to include its origin from the subclavian artery. The left circumflex coronary artery was dissected free from its origin from the mainstem left coronary artery to include a segment 3 to 4 centimeters in length. The internal mammary artery was divided distally and anastomosed end-to-end to the distal segment of the circumflex coronary which had been divided in its proximal centimeter (Fig. 1).

In group II there were 11 dogs in which a carotid artery autograft was taken initially and temporarily placed in saline solution. The left thorax was then opened and the circumflex coronary artery dissected free as in the first group of dogs. The previously removed carotid autograft was then prepared and anastomosed end-to-side to the proximal portion of the left subclavian artery. The distal end of the carotid autograft was anastomosed end-to-end to the distal end of the divided circumflex coronary as in the previous group of dogs (Fig. 2).

Continuous sutures of No. 5-0 arterial silk, utilizing both everting mattress and over-and-over stitches, were used in making the anastomoses in both groups of animals.

Adequate circulation was maintained to the peripheral segment of the divided circumflex coronary artery during the period of anastomosis by the use of a short intra-arterial polyethylene catheter (Fig. 3). The polyethylene catheter was placed in both the proximal systemic and distal coronary arteries and held in place by ligatures of heavy silk. It acted as a conduit for the animals' own oxygenated blood and as a stint over which an anastomosis could readily be made. To facilitate removal of the polyethylene tube a small silk traction-removal suture was placed in the distal end of the polyethylene tube. The ends of the traction removal suture protruded out between the vessel edges during the period of anastomosis. After placement of the last suture in the anastomosis, but prior to its being pulled taut to secure hemostasis and coaptation of the vessel edges, the polyethylene tube was easily removed through the site of anastomosis by pulling on the traction removal suture (Fig. 3).

Because of the difficulty of controlling the effects of anticoagulants in canine animals and the problems of management of their

associated hemorrhagic complications, anticoagulants were not used in these experiments. Every effort was extended to apply meticulous techniques and attain a precise approximation of the intimal surfaces at the sites of anastomosis. Avoidance of all unnecessary trauma to the systemic artery, autografts, or coronary vessels was practiced in hopes of maintaining patency of the anastomoses.

RESULTS

Nine of the animals, or 36 per cent of the entire series, succumbed within 24 hours following the procedure. In all 9 animals there was thrombosis at the sites of anastomoses or within the autografts. A second group of 10 animals, or 40 per cent of the entire series, survived for 1 to 3 days following the anastomoses or grafting procedures. In 2 of the latter 10 animals the graft was thrombosed, while in an additional animal the graft was only partially occluded by a thrombus. The remaining 7 animals were found to have widely patent anastomoses or grafts. The cause of death in the latter 7 animals was not immediately apparent but multiple punctate hemorrhages were seen throughout the myocardium supplied by the distal circumflex coronary artery. The etiology of these hemorrhagic areas or their influence on the ultimate death of the animals is not known at this time.

Of the remaining 6 animals, or 24 per cent of the series, which were considered long term survivors, only 2 were found to have patent functioning grafts 5½ and 6 months following anastomosis. Patency of the grafts was established by in vivo coronary angiograms (Fig. 4). The animals were subsequently sacrificed and the sites of anastomosis and the autografts were directly examined to confirm the findings of angiography (Fig. 5).

A comparison of the two groups of animals reveals that only 21 per cent of the internal mammary-coronary anastomosis were patent at the time of examination. In contrast, 55 per cent of the autograft-coronary anastomoses were patent at the time of examination. The carotid autografts were considerably larger vessels than the internal mammary arteries, and their caliber was equal to or greater than that of the coronaries, a factor which greatly facilitated their anastomosis and which may explain the more favorable results associated with their use.

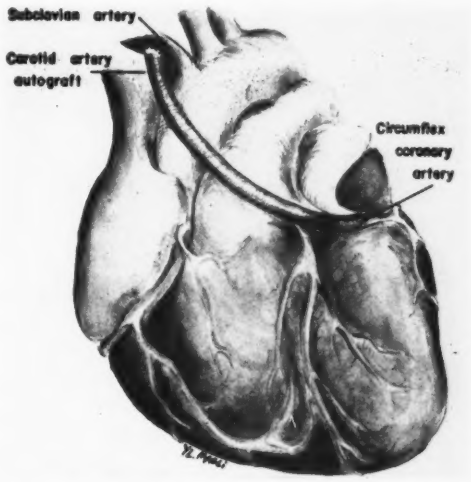

FIG. 2. Systemic-coronary anastomosis utilizing a carotid autograft between the left subclavian and circumflex coronary arteries.

DISCUSSION

Systemic-coronary anastomosis was actually attempted in animals as early as 1940 but was abandoned because of the frequency of associated ventricular fibrillation following division of a major coronary artery.

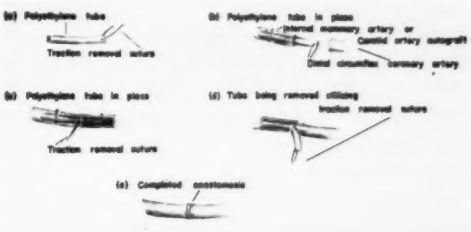

FIG. 3. Diagrams depicting use of a short segment of polyethylene tubing to maintain distal coronary arterial flow during periods of systemic-coronary anastomosis.

FIG. 4. In vivo coronary angiogram, performed 6 months following systemic-coronary anastomosis, revealed widely patent functioning carotid autograft maintaining circulation to distal circumflex coronary artery.

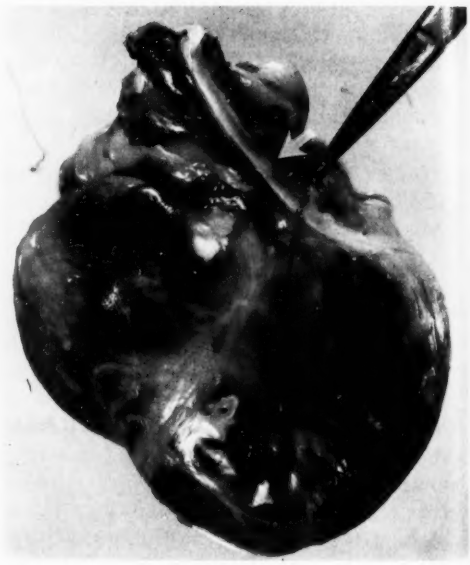

FIG. 5. Autopsy specimen revealing widely patent autograft and anastomosis (arrows). This animal was sacrificed 6 months following the systemic-coronary anastomosis.

Acute occlusion of the main trunk of the left circumflex coronary artery in dogs is regularly followed by ventricular fibrillation within 2 to 4 minutes, and has an accepted immediate mortality of greater than 70 per cent. It, therefore, became mandatory that the distal segment of the divided coronary artery be perfused with oxygenated blood during the periods of anastomosis. Various techniques of supplying oxygenated blood to the distal segment of a divided coronary during systemic-coronary anastomosis have been recently described. The technique utilized in these experiments was highly satisfactory and had the desirable factors of: (1) utilizing the animals' own oxygenated blood, (2) minimal trauma to the intimal surfaces of short segments of systemic artery, arterial autograft, and coronary artery, and (3) ease of removal of the polyethylene catheter at completion of the anastomosis.

In all 25 animals in this series a systemic-coronary anastomosis was successfully accomplished. At the time of completion of the procedures, there was neither gross nor electrocardiographic evidence of myocardial infarction. In spite of apparent adequate flow through the anastomosis or grafts at the completion of the procedure, minimal trauma to the intimal surfaces of the vessels and the grafts, and attempted meticulous and precise anastomotic techniques, the incidence of thrombosis in this series was considerable.

One could readily enter into an extensive theoretic discussion of various factors which might favorably alter the end results presented herein as well as those reported by others. However, it must be remembered that the systemic-coronary anastomoses performed in these experiments were done under optimum conditions with healthy animals, utilizing vessels which were free of disease. It is extremely dubious if the results reported herein, as well as those reported by other investigators, which in themselves leave something to be desired, could be achieved with similar procedures applied to diseased coronary arteries in man. Our ex-

periences with the experimental evaluation of systemic-coronary anastomosis preclude its clinical application in the surgical management of segmental occlusive coronary artery disease in man.

SUMMARY

Experiences with the experimental evaluation of a series of systemic-coronary anastomosis have been presented. Systemic-coronary anastomosis is technically feasible in the canine animal and, in certain instances, will maintain patency and distal coronary flow. The mortality associated with canine systemic-coronary anastomosis precludes, at this time, its clinical application in the management of segmental occlusive coronary artery disease in man.

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EDITORIALS

THE GASTRIC ANTRUM: FRIEND OR FOE?

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UNTIL RECENTLY, the accepted surgical treatment of medically resistant duodenal ulcer has been a three-quarter gastric resection with continuity restored by the Billroth II technique. To be sure, there was some controversy as to whether a long or short afferent loop should be left and whether the anastomosis should be made isoperistaltic or antiperistaltic. The basic concept, however, of extensive gastric resection and removal of the antrum was acknowledged. The functional results following this type of gastric resection such as occurrence of "dumping" and the inability of the patient to gain and maintain weight left much to be desired. Of the newer procedures recommended, segmental gastric resection, as described by Wangensteen and ourselves, that is, the retention of the antrum and its anastomosis to a residual gastric pouch has probably caused most perplexity. Edkins' concept that the antrum elaborates gastrin, a powerful secretagogue, has, after considerable controversy, been accepted. It is primarily to remove the source of gastrin that surgeons have believed removal of the antrum to be mandatory. It has been known too, that the antral exclusion operation for duodenal ulcer has been characterized by a high rate of recurrent ulceration. The seeming paradox of poor results with the antral exclusion operation and the good results reported to date with segmental gastric resection has to some extent been resolved by recent experimental work in a number of laboratories.

During the past 4 years a considerable body of evidence has accumulated to suggest that the antrum is capable of inhibiting gastric secretion provided acid comes into contact with the antral mucosa. This concept may explain why, when the antrum is excluded, results are different from when the antrum is anastomosed to a residual gastric pouch.

Dragstedt and his associates (6) have shown that the antral stimulation brought about by perfusion with liver extract could be prevented by making the perfusate strongly acid (*p*H 1). These investigators believe that acid in contact with the antrum mucosa inhibits gastric secretion solely by interfering with the elaboration or release of gastrin. Experiments, however, by Harrison and his co-workers as well as by Jordan and Sands have suggested the possibility that inhibition of gastric secretion may be due to elaboration of an acid-inhibiting hormone by the antrum.

The resolution of this problem is more than of academic interest. The mechanisms by which the gastric antrum brings about acid inhibition may have the greatest clinical significance. It would appear that greater attention to details such as cannulation of pouches, methods of irrigation, techniques of collection of gastric secretion, use of proper antral stimulating agents, and the performance of a sufficient number of experi-

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ments to insure statistical validity, may help resolve the differences that exist amongst various investigators.

The role of the vagus nerve too needs further consideration. Code and Watkinson showed that acid instilled into the duodenum could only inhibit the secretion of an indicator gastric pouch if it were innervated. May such not also be the case when antral inhibition is evoked? Studies of the role of the vagus nerve, therefore, in gastric acid inhibition by the antrum are very definitely needed.

The gastric antrum is indeed a "controversial" organ, but continued study of its function may well lead to important information regarding regulation of gastric secretion by the stomach itself and may open new avenues to the treatment of medically resistant duodenal ulcer.

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WHY DO CANCER PATIENTS DIE?

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IT IS USEFUL to re-examine from time to time the status of our knowledge of a disease. It will be the purpose here to examine the mechanism of death from cancer. Of course, in few diseases has the ultimate cause, the ultimate lesion in terms of cellular biochemistry and physics, been defined. Nevertheless, in asphyxia due to laryngeal obstruction the resulting anoxia serves as a reasonably sharp and readily demonstrable reference point. In death from terminal cancer, in contrast, no such obvious pathophysiology may be discerned. In fact, the cause of the "malignant cachexia" may be almost completely obscure. Certainly no major organic function need be grossly interfered with.

It is not necessary to consider in detail here the possible cause or causes of cancer. The theories of "spontaneous" multiple mutations, of initiating and promoting factors, of critical cell colony size and growth restraint, chronic irritation by carcinogens or predisposing diseases, or even the theory of viral etiology—all these are of much interest in the genesis of the original or primary tumor, but they do not explain how the tumor, once formed, kills the host.

Since it is not so often the primary tumor as it is the metastases which render a cancer beyond eradication by surgery, one might be tempted to conclude that it is the metastases which kill the patient. But if so, which ones—contiguous spread, lymphatic, or blood-borne? Actually, in recent years, studies have shown that the venous drainage of the tumor and even distant systemic blood may contain many embolic cells. But do these cells per se produce death and, if so, how? They probably do not, at least not by mechanical means, though they may contribute to the total biochemical impact of the malignancy.

More and more the concept of individual host immunity to cancer has come to be accepted. All of us can recall patients whose tumor had grown slowly for months or years, only to metastasize widely shortly following surgery at which the primary neoplasm was incompletely excised. A patient with a malignant ulcer in a burn scar, present for years, suddenly exhibits widespread metastases a few weeks following complete local excision. Another: We recently observed the development of mucous adenocarcinoma in the operative scar 15 years following resection of a primary carcinoma of the colon. What forces had held these cancer cells dormant or at least in check for so long? The forces were probably immunologic in nature, for recently the existence of a relationship between host resistance and tumor implants has been firmly established in controlled animal experiments. Thus we may at this point list at least one factor by which the tumor begins to overpower the patient, namely, that the aggressive "biologic activity" of the tumor breaks through the immunity of the host. Yet even this statement scarcely would satisfy the experimental biologist. How does the malignant process overpower the biochemical defenses of the host? Moreover, is there evidence that tumors do produce demonstrable biochemical lesions, perhaps at an enzymic and, ultimately, a molecular level? There is.

While the most consistent biochemical lesion found in cancer is a reduction in liver catalase activity in the presence of rapidly growing tumors, certain clinically perceptible alterations are now known to be associated with certain tumors. The hypersecretion of some endocrine tumors represents a special case and need not be considered here. Carcinoma of the lung or

pleura may produce distant bone and joint changes, or hyponatremia, or gynecomastia. Carcinoma of the lung and kidney, among others, may produce hypercalcemia even in the absence of demonstrable bone lesions. The carcinoid tumor may result in the now well recognized "carcinoid syndrome" with serotonin crisis. Carcinoma of the prostate may be associated with excessive fibrinolytic activity as well as with an elevation of the acid phosphatase level. Certain localized ovarian tumors produce pleural effusion in the absence of ascites. And many tumors result in rapid anemia, fever, leucocytosis and general malaise.

Other examples of systemic biochemical alterations in cancer could be cited but those mentioned will suffice. One need no longer anticipate a death due in large part to mechanical interference with a vital function or to hemorrhage and infection. The far advanced tumor, whose hallmark is the "cancer facies" which accompanies the malignant cachexia that all physicians know so well, undoubtedly influences the host in a great variety of subtle biochemical ways, as does extensive sepsis. Perhaps the appetite is lost (through effects upon the hypothalamus?) and starvation is a prominent part of the pathology of advanced cancer. Nevertheless, many experiments have dealt with the force-feeding by tube of patients whose cancer starvation was not due to alimentary tract obstruction. Such efforts have often been unsuccessful in achieving nutritional rehabilitation. Clearly, biochemical derangements would appear to exist which preclude the effective metabolic use of the nutrients ingested.

Cancer therapy usually takes the form of a surgical, physical (by radiation), or chemotherapeutic attack upon the primary tumor and its metastases. Perhaps in the near future we may even witness a practical immunologic attack against the malignant disease, regardless of whether it is viral in origin or not. But looking toward the target of the biochemical aggression again, the normal host cell, might it not be possible to do more toward protecting the host cells from the metabolic effects of the tumor? This might provide considerable symptomatic and even therapeutic palliation. There is precedent for this in the instance of certain endocrine tumors. For example, hyperinsulinism due to functioning metastases of carcinoma of the isles of Langerhans has been controlled by both cortisone and glucagon therapy. It is not inconceivable that, long before we have a chemotherapeutic agent that will eradicate the tumor itself, agents may be found which achieve long range palliation through biochemical interposition.

In summary, surgical thought has been widened, deepened, and extended to embrace the concept of cancer as a systemic or biochemical disease, radiating initially from a single focus but later from metastases as well. It is admissible in surgical circles now that both surgery and radiation are frequently inadequate and, of course, cancer chemotherapy is in its infancy. However, above all, our concepts have been developed to the point that cancer is clearly recognized for the metabolic agressor that it is. The cause of death in the presence of far advanced cancer is an extensive derangement of normal biochemical functions and, in this respect, the similarity between malignant disease and sepsis is once again underscored.

THE SURGEON AT WORK

TECHNIQUE OF SIGMOIDOCYSTOPLASTY

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ILEOCYSTOPLASTY, the operative procedure previously described (3) to enlarge or replace a portion of diseased bladder, has found enthusiastic acceptance and general use. Its usefulness and importance seem well established.

By contrast, sigmoidocystoplasty, the somewhat simpler and in some ways more appealing procedure for enlargement of the urinary bladder, seems to have gained little attention or recognition either in this country or abroad.

In 1948, Rubin successfully substituted for the urinary bladder in dogs isolated segments of the sigmoid colon. He reviewed the literature on the subject to that date. Subsequently, Bisgard and Kerr reported similar experience with animals. In all these experiments, the procedure involved ureterosigmoidostomy as part of the operation and thus increased the operative difficulties encountered.

Shoemaker and Marucci mentioned this procedure and experimentally applied the reversed seromuscular graft to the bladder by using segments of sigmoid. Leadbetter and Shaffer increased the bladder capacity by use of the cecum. Early results were technically satisfactory, but later, retention led to cutaneous diversion of the urine. Menville and associates recently described their success with this procedure.

It seems that Lloyd Lewis alone among current American authors, has applied the procedure to be described herein.

From the Department of Surgery, Division of Urology, University of California Medical Center, and the Wadsworth Veterans Administration Hospital, Los Angeles, and the Los Angeles County Harbor General Hospital, Torrance, California.

Animal experiments basic to this work were supported by The Fund for the Advancement of Urology and the Bay District Surgical Society.

Our own interest in the experimental and clinical applications of bladder enlargement and substitution with isolated loops of sigmoid colon (maintaining the integrity of the normal trigone of the bladder) began in 1953 with animal experiments (2, 9).

The technique we have employed to increase bladder capacity utilizing isolated segments of sigmoid will be described in detail in this article. Results of this operation in 4 patients are to be described elsewhere in detail. To date, experience with this procedure has been too limited to allow us to make a suitable comparison between the results of sigmoidocystoplasty and ileocystoplasty. Since the sigmoid colon lies close to the bladder and may be anastomosed to the back of it without serious anatomic relocation of intraperitoneal viscera, and since the colon has a thick muscular coat and most people are able to identify the sensation of a full colon, it may be that this organ is best suited to perform the function of bladder enlargement. Although considerable data have been amassed concerning absorption of urinary constituents from the mucous membrane of both the colon and the ileum, suitable comparisons do not exist. It might be expected that there would be less total absorption from the colon.

TECHNIQUE

The abdomen is opened through a lower midline incision.

Intraperitoneal organs are lifted upward exposing the sigmoid colon and the back of the bladder. The peritoneal reflection is cut vertically in the midline over the back and posterior surface of the bladder and is bluntly stripped

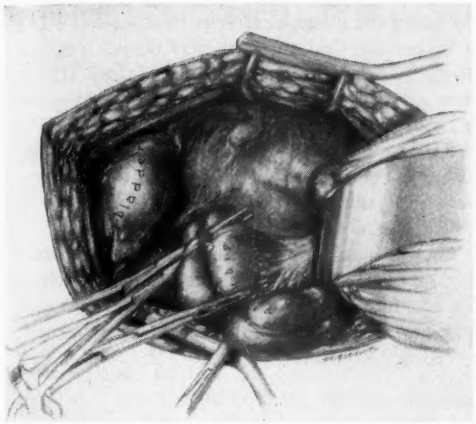

FIG. 1.

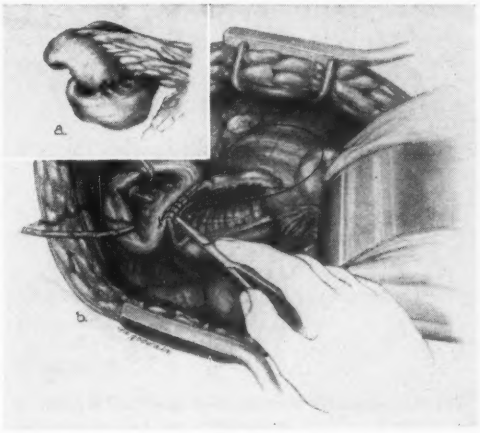

FIG. 3.

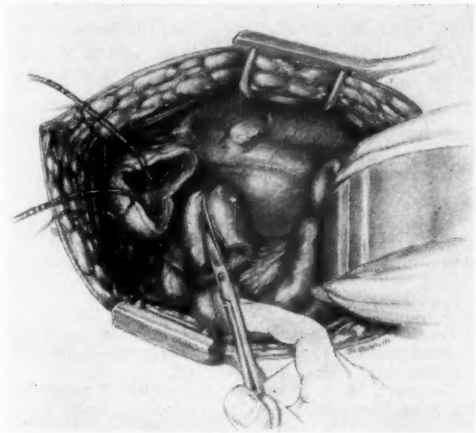

FIG. 2.

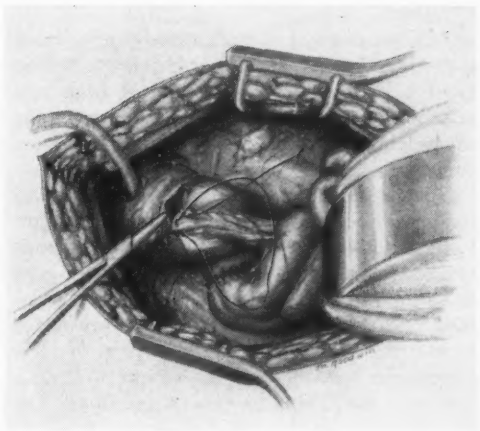

FIG. 4.

FIG. 1. The sigmoid colon is pulled upward, and a 10 to 15 centimeter redundant segment conveniently close to the bladder is isolated.

FIG. 2. Normal bowel continuity is re-established by sigmoidosigmoidostomy. The isolated segment of colon is opened on its antimesenteric border. The bladder is opened in its dome.

FIG. 3. The isolated sigmoid patch is sutured to the opened bladder.

FIG. 4. Adequate catheter drainage is provided. The sigmoid patch is fitted to the dome of the opened bladder.

off the posterior wall of the bladder down to a point near the trigone.

The sigmoid colon is pulled upward from the pelvis and a redundant portion conveniently close to the bladder is identified. A 10 to 15 centimeter segment of sigmoid colon is isolated, with care to allow easy reapproximation of the remaining colon to establish normal continuity (Fig. 1).

It is neither necessary nor advisable to cut deep into the sigmoid mesentery.

Bowel continuity is re-established, posterior to the isolated segment by sigmoidosigmoidostomy using 2 layers of sutures. Continuous catgut is used for the inner, mucosal layer and interrupted silk for the muscularis and serosa.

The isolated sigmoid segment is irrigated until free of all fecal material and mucus. Then it is opened on its antimesenteric border so that it forms a flat "patch" (Fig. 2).

The bladder is opened with a midline incision at its vertex. The ureteral orifices are catheter-

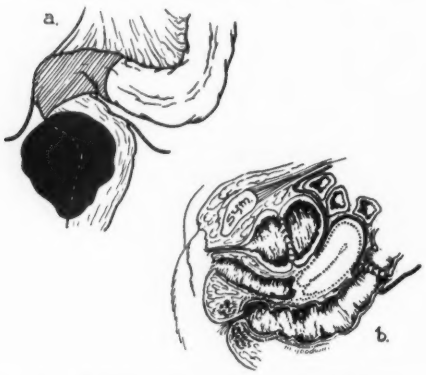

FIG. 5. a, Relative position of bladder and segment of sigmoid to be utilized. b, Sagittal section showing operation completed.

ized for purposes of identification. The opening in the bladder is extended anteriorly to within about 5 centimeters of the vesical neck and posteriorly to within 3 to 5 centimeters of the ureteral orifices. It is important not to go too close to the trigone (Fig. 3).

The open patch of sigmoid colon is now anastomosed directly to the opening in the bladder. A continuous No. 000 chromic catgut suture is used for the inner layer. All the layers of bowel are sutured to all the layers of bladder and every third or fourth suture is locked to prevent a purse-string effect. A second outer layer of a few interrupted No. 00 chromic catgut sutures is used after the closure to prevent tension on the suture lines (Fig. 4).

Before the opening in the bladder is completely closed with the sigmoid patch, a mushroom or Malecot catheter is placed through a stab wound in the intact anterior bladder wall and a urethral catheter is introduced as well (usually from inside out by passing the external end of a Malecot catheter outward on the end of a urethral catheter which has been passed from the inside out). Continuous drainage from these catheters is important because of a mucus formation during the postoperative period. It is not presumed that the suture line is watertight.

The new bladder patch is loosely extraperitonealized, as much as is easy to do, by suturing the peritoneal flaps to the sides of the patch and its mesentery. The abdominal wound is closed in layers. The prevesical space is adequately drained on both sides (Fig. 5).

During the postoperative period, care is taken to be certain that the catheters do not become plugged with mucus or with blood clots. Irrigations are kept at a minimum unless there seems to be occlusion of one or the other catheter, in which case gentle irrigations with not more than 30 cubic centimeters of saline solution are employed. Both catheters are left in place for at least 2 weeks postoperatively.

The patient is then able to resume a normal voiding habit and the sensation of fullness, which is a combination of bladder and sigmoid colon sensation, is similar to that to which the patient is already accustomed.

RESULTS

The procedure described has been employed in 4 patients. The first was treated surgically in 1955. In each case the operation has been technically satisfactory. In 2 cases in which it was employed for vesicovaginal fistula, the fistula recurred. No deaths and no serious complications have resulted. The detailed results are to be reported elsewhere.

SUMMARY

A technique of sigmoidocystoplasty for enlargement of the urinary bladder is described.

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A SAFE METHOD FOR ATRIAL ENTRANCE IN THE TREATMENT OF MITRAL STENOSIS

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Los Angeles, California

SURGEONS have described their experiences with serious or even fatal hemorrhage while doing a mitral commissurotomy for the treatment of mitral stenosis. In 1957, Morris and Haight described a method of treating atrial tears once they occur. This consists of placing a balloon catheter into the atrium through the tear, inflating the balloon, and pulling it up against the atrial wall. This procedure tamponades the bleeding area while sutures can be taken in the wall. The procedure certainly has merit and at times may constitute a life-saving method.

The method which we have employed of entering the atrium is herein described. Because of the safety of this technique we now routinely use it for all mitral commissurotomies whether the operative procedure is the initial one, whether it is for a second operation, whether the atrium is filled with clots, or whether the procedure is done from the right side.

From the Department of Surgery of the University of Southern California School of Medicine and St. Vincent's Hospital, Los Angeles. Aided by grant from American Heart Association.

TECHNIQUE

The technique consists of placing a series of 3 interrupted mattress sutures of No. 2 silk in the atrial wall or the atrial appendage. Tangential stitches of No. 2 silk are placed at each corner. A small incision is then made with a knife (Fig. 1). This is the only time one may encounter difficulty and, therefore, care must be taken not to cut the sutures posteriorly. After the initial incision is made, it is enlarged with a scissors until it will admit the index finger. After inserting one's finger, the sutures are pulled tight thereby obtaining complete hemostasis. After the commissurotomy is completed the finger is removed and the sutures are pulled taut by the assistant. The sutures may be tied or they may be

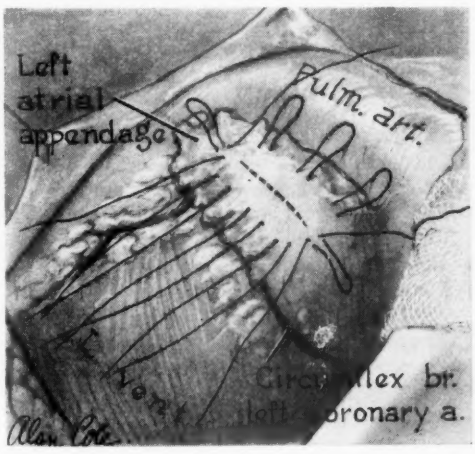

FIG. 1. Placement of a series of interrupted mattress sutures in the atrial appendage and wall and the line of the incision.

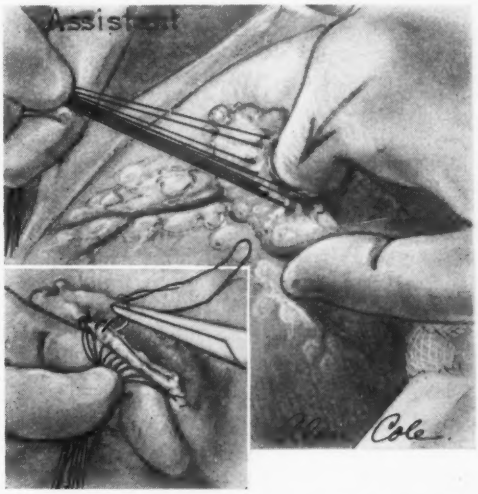

FIG. 2. Insertion of index finger. Inset shows sutures pulled taut and the incision in the atrial wall being closed with a continuous suture.

removed after the incision has been closed with a continuous stitch of No. 00 silk.

This method is of particular benefit when there is no appendage due to previous operation or when there is a congenitally small appendage. If the appendage is full of clot an area on the atrial wall may be chosen for safe insertion of one's finger or a knife, if necessary.

CONCLUSION

We believe this method is superior to placing a purse-string suture around the base of the appendage for several reasons: (1) If the purse-string suture is not tied snugly, a thrombus may form in the appendage postoperatively with the danger of peripheral embolization. (2) If the appendage is full of clots, it is safer to enter the atrial wall than attempt to enter the appendage with the danger of producing embolization. (3) There is no danger of tearing the atrial appendage if the appendage is small.

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AN IMPROVED METHOD OF VENOGRAPHY

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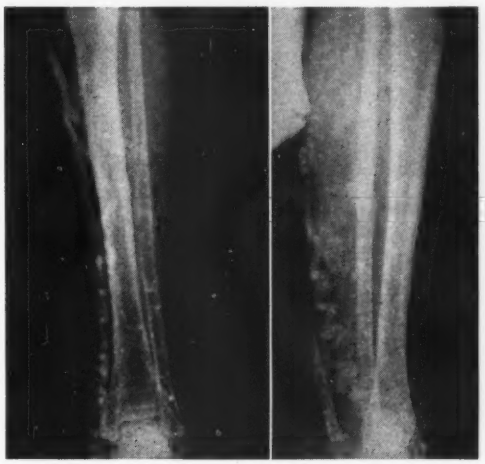
MILTON GINSBERG, M.D., F.A.C.S., Fort Howard, Maryland

A SATISFACTORY METHOD of venography should permit filling of the necessary veins without layering and should produce good contrast in the roentgenograms. Injection of the medium should be innocuous to the patient and easy for the doctor. It should be possible to take the roentgenograms at a leisurely pace without exposure of the medical personnel to the roentgen rays.

A continuous intravenous infusion of a dilute solution of a contrast medium will fulfill these criteria. The solution is administered over a long enough period of time so that anteroposterior, lateral, and stereoscopic views, if they are desired, can be made.

A solution of 14 per cent urokon is made by mixing 50 milliliters of a 70 per cent solution of urokon with 200 milliliters of physiologic saline in a bottle designed for the administration of fluids intravenously. Ten milligrams of chlortrimeton maleate (chlorprophenpyridamine maleate) in 1 milliliter of distilled water are added to the mixture to decrease the possibility of a generalized reaction to the urokon. A standard assembly with a tube for infusion and an air vent is attached to the bottle. Air injected through the vent will be retained within the bottle and will increase the pressure within the bottle.

The patient is placed in a supine position on the table which is used to make the roentgenograms. The head of the table is raised to about 65 degrees from the horizontal. A sandbag is placed under the heels of the patient. A venipuncture, using a No. 20 French gauge needle, is performed as distally as possible on the lower part of the leg or foot. If only veins small in caliber are present, a No. 25 French gauge needle may be used. When a venipuncture cannot be done, a small incision is made over the greater saphenous vein over the ankle joint, and a No. 16 French polyethylene catheter is introduced into the vein. A No. 16 French gauge needle is inserted into the end of the catheter and serves to connect the catheter and the polyethylene tube leading from the bottle. Infusion is started; the tourniquet is removed. The legs of the patient are rotated inwardly so that the shadows of the deep veins will not be superimposed upon those cast by the tibia and the fibula. The solution is administered under a slight degree of pressure by the injection of air into the bottle through the air vent. Enough air is injected so that a stream of the solution flows through the modified Murphy drip of the assembly. If a No. 25 French gauge needle is used, the pressure is increased to cause a rapid flow of drops, but not a stream. If a small needle is used for the venipuncture the pressure should not be raised to a height to produce a stream since the bottle might break. When 100 milliliters of the solution have entered the vein, the flow is decreased to about 120 drops per minute and is maintained at that rate throughout the remainder of the procedure. An anteroposterior roentgenogram, which is made on a



a b

FIG. 1. This patient complained of an ache in the left leg and edema about the left ankle joint. Note superficial varicose veins and normal deep veins in the: a, anteroposterior view of the left leg; b, lateral view of the left leg.

From the Surgical Service, Veterans Administration Hospital, Fort Howard, Maryland.

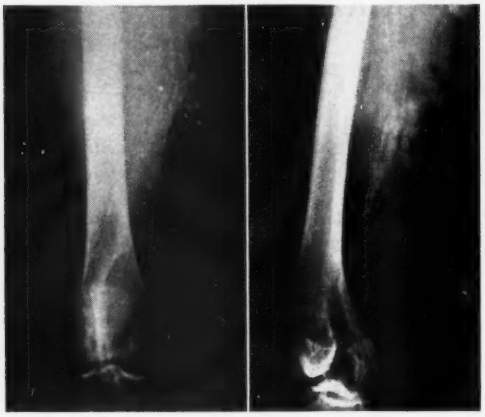


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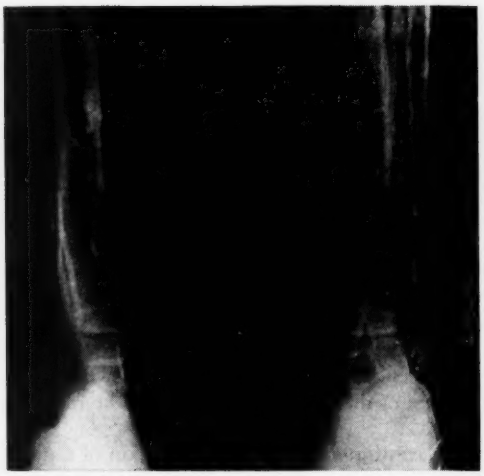
Fig. 2.



a

a b

Fig. 3.

b

Fig. 4.

FIG. 2. This patient had an infection of long standing and recent edema of the left leg. Note varicose veins of left thigh below the skin in the: a, anteroposterior view of left thigh; b, lateral view of left thigh.

FIG. 3. This patient had pain and edema of the right leg. Note normal veins in the: a, anteroposterior view of right leg; b, anteroposterior view of right thigh.

FIG. 4. This patient had pain in the left and right legs. Venograms of both legs were done simultaneously. Note varicose veins of both legs in the: a, anteroposterior view of the lower parts of left and right legs; b, anteroposterior view of upper parts of left and right legs.

14 by 17 inch film, is taken of the lower part of the leg and then of the upper. In large patients, it may be necessary to make a third exposure of the region of the knee. The patient then slowly turns about 90 degrees so that the leg being studied is against the table. By flexing the lower leg upon the upper, it is possible to obtain an unobstructed view of almost the entire lateral aspect of the leg. Roentgenograms of the leg in the lateral position are then made. The patient turns to the original position and a scout roentgenogram of the abdomen is taken for visualiza-

Fig. 5.

Fig. 6.

FIG. 5. This patient had edema of the right lower extremity from partial compression of the right common iliac vein by a carcinoma of the bladder. Note collateral veins of pelvis and wall of lower part of abdomen in anteroposterior view of right pelvis and right thigh.

FIG. 6. This patient had edema of the right leg. The recanalized deep femoral vein and the collateral veins are demonstrated in the anteroposterior view of the right thigh.

tion of the veins of the pelvis and of the wall of the lower part of the abdomen. An evaluation of renal function may be made from the roentgenogram also since an excretory pyelogram of sufficient diagnostic accuracy is occasionally obtained. The administration of the solution intravenously is discontinued before the solution is completely used since air under pressure is present in the bottle and might enter the vein causing an embolism from air when the fluid is gone. The patient is returned to the horizontal position. The needle or catheter is removed from the vein of the leg.

Venography has been done in 25 patients with excellent results and without a local reaction. The results in some of these patients are shown in Figures 1 through 6. The anterior tibial, the posterior tibial, and the popliteal veins were seen in 24 of the 25 patients. The superficial femoral vein was visualized in 23 patients. The deep femoral vein was seen in only 5 patients, and in 2 of these the superficial femoral vein was recanalized and a number of collateral veins were seen to join that vein. In 2 patients who were suspected of having compression of the common iliac veins due to a tumor in the pelvis, a collateral venous circulation to the abdominal veins was demonstrated.

A local reaction to the urokon was not seen. Extravenous injection of the drug should be avoided or inflammation will occur. Thrombophlebitis did not follow the injection of this solution of urokon. A transitory generalized flush of the skin of the patient was not detected. A generalized feeling of warmth did not follow the injection. Nausea and vomiting occurred in 5.

In 1 patient a bilateral venogram was done. This procedure is not recommended since it is difficult to regulate the flow of solution so that the veins in both lower extremities are visualized equally well. The examination of each leg should be done at separate times.

The patient is tested for sensitivity to urokon when the infusion is started by permitting 1 or 2 cubic centimeters of the drug to run into the vein. The patient is then observed for 3 minutes. If signs of a reaction do not appear, the remainder of the solution is injected.

SUMMARY

A continuous intravenous infusion of a 15 per cent solution of urokon has permitted an improved method of venography. The roentgenograms can be taken at a leisurely pace without exposure of the medical personnel to the roentgen rays.

THE SURGEON'S LIBRARY

Reviews of New Books

WITH THE SECOND EDITION of the fairly brief monograph, *Lumbar Disc Lesions*,[1] Dr. Armstrong has cut a welcome clearing through the ever thickening fog which surrounds the subject of pathologic discs. Based upon careful clinical observation and treatment of over a thousand patients, the book is direct, didactic, pointedly repetitive, authoritative, and honest. A large portion of the book is concerned with the anatomic nature of the lumbar discs and the pathologic anatomy which is the basis for the "herniated nucleus pulposus." The typical history and findings upon physical examination are thoroughly discussed, and there is an excellent section on differential diagnosis, which must involve a rather large number of fairly common conditions. The author does not recommend routine myelography, and it is heartening to read that he decries discography altogether. He advocates conservative treatment at first, meaning bed rest with immobilization and traction if they are considered hopeful, but once surgery is indicated by the failure of such treatment, he insists that it must not be delayed. He is an orthopedic surgeon, but he does not recommend routine spinal fusion after the removal of a defective disc. He emphasizes the point, too, that while surgery often immediately and permanently relieves the sciatica, it may by no means prevent the development of progressive lumbar instability, pain, and disability.

Armstrong has charitably omitted all meaningless and boring charts showing "percentages of cures" or "incidence of lesions according to age, sex, occupation, and anatomic level." The book is beautifully and extensively illustrated; many illustrations are in full color. The bibliography is large and up to date. It is only to be hoped that this valuable book will find its way into the hands not only of young neurosurgeons and orthopedic surgeons, but also of some of the "old masters" as well. —*John Martin.*

THE SECOND EDITION of *Clinical Endocrinology*[2] appears at this time because the authors realized the great expansion of knowledge in several areas of endocrinology that has taken place since the first edition was published a few years ago. They have made extensive revision of virtually all sections and completely rewritten certain chapters. New material is presented concerning the pathology and therapy of diseases of the thyroid and adrenal glands, the use of long acting progesterone derivatives, and the classification and diagnosis of testicular failure.

In the first edition the authors pointed out that endocrinology has developed from a rather disreputable stepchild of medicine into a highly respected and dignified member of the family of medical specialties. In this second edition, as in the first, each gland is discussed from the standpoint of embryology, anatomy, histology, physiology, pathology, pathologic physiology, diagnosis, and treatment. The last chapter deals with procedures and methods of study, since the co-operation of the attending physician is necessary for the satisfactory performance of certain laboratory studies. The indications for specific tests, collection of specimens, description of methods together with normal and abnormal variations of possible results are given in moderate detail. Ten pages at the end of the text list commercial hormone preparations with their trade names, route of administration, and remarks concerning their clinical use which should be helpful and time saving.

The bibliography at the end of each division refers the reader to recent, stimulating, and comprehensive discussions and critical reviews. A most complete index enables one to secure information readily from the text.

This is an easy to read, up-to-date textbook on endocrinology. The undergraduate student will find that it is easily read when chapters are taken in order. The practicing physician will find not only the best approaches to diagnosis and advice regarding effective therapy, but a concise explanation of the rationale underlying the diagnostic procedures and therapeutic recommendations. —*George C. Turnbull.*

THE SMALL "PRIMER" in anesthesiology, *Narkose-Fibel*,[3] has no pretensions to replace the larger texts. Nevertheless, it is surprising how much information can be presented in concentrated form if all extraneous material is avoided and only the essentials re-

[1] LUMBAR DISC LESIONS; PATHOGENESIS AND TREATMENT OF LOW BACK PAIN AND SCIATICA. By J. R. Armstrong, M.D., M.Ch., F.R.C.S. Foreword by H. Osmond-Clark, C.B.E., F.R.C.S. 2nd ed. 244 pages, illustrated. $12.00. Baltimore: Williams & Wilkins Co., 1958.

[2] CLINICAL ENDOCRINOLOGY. By Karl E. Paschkis, M.D., Abraham E. Rakoff, M.D., and Abraham Cantarow, M.D. 2nd ed. 941 pages, 198 illustrations. $18.00. New York: Hoeber-Harper Book, 1958.

[3] NARKOSE-FIBEL. FUR KLINISCHE UND AMBULATE OPERATIVE EINGRIFFE. By Dr. med. H. J. Thum, Bochum. Foreword by Prof. Dr. med. H. Burkle de la Camp. 103 pages, 10 illustrations. $3.20. Stuttgart: Georg Thieme, 1958.

tained. Included are various forms of anesthesia; physiology of anesthesia; premedication; various anesthetic agents; physiology and treatment of shock and collapse; anesthesia in diseases of brain, circulatory system, lung, liver, kidney, endocrine glands; anesthesia in thoracic, abdominal, pediatric, dental, maxillofacial, eye, ear, nose, and throat, geriatric, and neurosurgery; anesthesia in diagnostic procedures. Recent agents and methods are well described—muscle relaxants, hypotensive anesthesia, etc.

The reader misses a more explicit presentation of the various forms of local, topical, and conduction anesthesia. Even for the various instrumental examinations the author seems to lean toward general anesthetic procedures. In this booklet everything is treated briefly, however comprehensively, and includes all the pertinent and important facts. An exhaustive index is included.

This little text can be recommended especially for the medical student and for the busy practitioner wishing to review the essentials of anesthesiology without going into details. —*Gunars Medins.*

THE REPORT of an international inquiry[4] to 69 eminent urologists by Prof. Franco de Gironcoli concerning their attitudes toward early surgical intervention in prostatic hypertrophy is published in the volume entitled *Early Prostatectomy?*. In the early days of prostatic surgery with its alarming mortality and high morbidity, operation was performed only when the symptoms were severe and the amount of residual urine was great.

With improvements in surgical technique, the mortality and morbidity have been lowered to a point where the operation need no longer be considered unduly hazardous. Hence, it is more often performed at a much earlier stage of the disease and most of the eventual complications of untreated prostatism with its inevitable train of infection, hydronephrosis, stone formation, and finally fatal uremia are prevented.

Although a few urologists still lean toward an ultra conservative approach to the problem and demand severe symptoms and a sizable residual urine before operating, the great majority prefer early surgery. Definite evidence of obstruction and not the volume of the residual urine is the operative criterion for most of the urologists questioned.

Interesting in this regard is the answer of N. L. Shepperd in favor of or against early surgery as follows: in 1930, absolutely no; in 1940, probably yes; in 1950 and onward, yes.

The introduction and conclusions of the inquiry are published in Italian, German, and English. The summaries of the individual answers are presented in English. —*Frederick A. Lloyd.*

THE AUTHORS of the monograph *Head Injuries*[5] are well known for their many publications having to do with the various aspects of cranial trauma, and particularly for their "stresscoat" method of study of the mechanism of such trauma. This book is apparently the summation of their extensive experiences, with both civilian and military types of injuries, and it ranges over a wide number of topics: a brief history of head injuries; cranial-intracranial anatomy; diagnostic techniques; clinical manifestations, complications and delayed sequelae, head injuries in children, head injuries in sports, the medicolegal aspects of head injuries, the surgical, nonsurgical, and general care techniques of head injuries, and others.

This book is an expression of the impressive experience of the authors in a favored subject, an experience which must be, and is, respected by contemporary neurosurgeons. A long bibliographic list follows each chapter, and in the text various authors are quoted freely along with their own practices. There is nothing particularly revolutionary in the authors' methods of diagnosis and treatment of head injuries, but their discussion of the mechanism of injury is fresh and thought-provoking as their reports on this subject have been for the past several years. One small criticism is that the second chapter, on normal cranial anatomy, could have been omitted without loss to the book, for regional cranial structures and relationships are discussed later in conjunction with descriptions of pathology. This book is a comprehensive, sound, and practical guide, modern in its outlook, positive but conservative in its recommendations for treatment. One of its brightest features is the magnificent illustrations. —*John Martin.*

ONCE AGAIN we have 3 fascicles from the *Atlas of Tumor Pathology*[6] Fascicle 2, *Tumors of the Skin* by H. Z. Lund; Fascicle 20, *Tumors of the Esophagus* by A. P. Stout and R. Lattes; and Fascicle 25, *Tumors of the Liver and Intrahepatic Bile Ducts* by H. A. Edmondson. As we have come to expect, these fascicles deal with each subject in an orderly and thorough manner and the illustrations, particularly the black and white photomicrographs, are exceptionally good. The authors also have given consideration to other common lesions that may be confused with the neoplasms of the respective organs. These volumes will be a worthwhile addition to the others in the *Atlas* and offer unusually good value for the small price.

—*William B. Wartman.*

IN THE PAST 18 to 20 years there has been renewed interest and, as a result, much progress in the field of prosthetics. Special research centers, new devices, better materials, sound physiologic principles, and better rehabilitation instruction have resulted in a new horizon for the person with the crippled or absent limb.

[4]EARLY PROSTATECTOMY? INTERNATIONAL INQUIRY. By Franco de Gironcoli. 229 pages, 18 illustrations. Treviso: Edizioni di Urologia, 1958.

[5]HEAD INJURIES; MECHANISMS, DIAGNOSIS, AND MANAGEMENT. By. E. S. Gurdjian, M.D., and J. E. Webster, M.D. 482 pages, 108 illustrations. Boston and Toronto: Little, Brown & Co., 1958.

[6]ATLAS OF TUMOR PATHOLOGY. Section I—Fascicle 2, Tumors of the Skin. By Herbert Z. Lund, M.D. 330 pages, 265 illustrations. $3.00. Section V—Fascicle 20, Tumors of the Esophagus. By Arthur Purdy Stout, M.D., and Raffaele Lattes, M.D. 105 pages, 58 illustrations. $1.00. Section VII—Fascicle 25, Tumors of the Liver and Intrahepatic Bile Ducts. By Hugh A. Edmondson, M.D. 216 pages, 207 illustrations. $2.25. Published under the auspices of the Subcommittee on Oncology of the Committee on Pathology of the Division of Medical Sciences of the National Academy of Sciences. Washington, D. C.: Armed Forces Institute of Pathology, 1957 and 1958.

The recently published book entitled *Functional Bracing of the Upper Extremities*[7] encompasses the stated field in a splendid manner. Now a single volume, one may find muscle and tendon function outlined, indications for various brace types, and, best of all, simple illustrations showing step by step construction of the appliances.

Surgical procedures for the rehabilitation of the upper extremity are many and often ingenious. There are, however, countless arms and hands rendered useless by illness or injury which are beyond surgical repair. The application of a splint to a poorly functioning extremity, utilizing a working limb as an activator, can frequently restore a member to some percentage of its former usefulness.

Often, splints on hands are used preoperatively and postoperatively to help regain motion or position. In this book assistive devices for most situations can be found. Admittedly, all splint designs could not be included. Those described have served well in the large centers throughout the country.

The text will undoubtedly be of interest to those physicians, physiotherapists, brace makers, and others whose talents are combined in an effort to restore form and function. —*William B. Stromberg, Jr.*

A VERY INTERESTING SERIES of papers presented at a 2 day symposium in July 1957 at Hammersmith Hospital, London is published in a volume entitled *A Symposium on Non-Toxaemic Hypertension in Pregnancy*.[8] Participants include outstanding obstetricians, internists, physiologists, and pathologists, most of whom are British.

Considerable experimental data are presented. A very practical section concerns the management of pregnancy complicated by hypertension, well documented by statistics. Though the title belies it, there are many remarks pertinent to pre-eclampsia and eclampsia. Considerable attention is also given to prognosis in hypertensive women who become pregnant.

This book is a worthwhile addition to the library of all who teach obstetrics, especially those responsible for residency teaching and internists who serve as consultants in obstetrics. —*Charlotte Herman Kerr.*

THE SIXTH EDITION of *A Method of Anatomy*,[9] a widely used textbook of human anatomy, has been published. In 21 years it has become, perhaps, the outstanding regional anatomy to appear in the English language. In the present edition, the text has been revised to include new material, largely of clinical significance, some 34 new illustrations, and a selected list of references. A further important revision is the use of the new anatomic nomenclature (*Nomina Anatomica Parisiensia*, 1955). Details of the central nervous system and histology have been largely omitted.

The organization of the subject matter is the same as in the fifth edition. A general section precedes the main regional sections which are: upper limb, abdomen, perineum and pelvis, lower limb, thorax, and head and neck. A closing miscellaneous section presents a discussion of the autonomic nervous system, body types, and bones of the skull, pectoral girdle, and wrist. This book is easily adaptable to a variety of dissection sequences since the regional presentations are tied in by cross references to other contiguous regions.

The abundant illustrations consist of line drawings and diagrams, noteworthy for their simplicity and clarity. One of the chief features which distinguishes this volume from the usual anatomy texts is that its objective is the comprehension of principles, and from this standpoint it proceeds to a correlation and understanding of anatomic facts. A corollary aim is to make anatomy interesting and of practical value. In the accomplishment of these goals the author has succeeded admirably. This textbook is well written, and the print is clear and easy to read. The binding is strong and the cover is both attractive and durable. It is recommended for medical students in anatomy and for advanced students and practitioners who may wish to restudy regional human anatomy.

—*William T. Kabisch.*

THE THORACIC SECTION of *A Stereoscopic Atlas of Human Anatomy*[10] by D. L. Bassett, Associate Professor of Anatomy, Stanford University, represents another important step toward completion of a praiseworthy endeavor of impressive magnitude. Like the antecedent sections, this current treatise in the comprehensive series is executed with technical skill and presented with artistic judgment. The series offers opportunity for convenient review of dissection. Each dissection represents a step in a series in a carefully planned succession; each is seen in full perspective, and in the coloring of admirably prepared laboratory specimens.

A fully labeled sketch, based upon a tracing of the original photograph, furnishes a topographic "map" for each view; consequently, they are not marred by pins, numbers, or guidelines. The set is compact, the views readily accessible; they may be regrouped to answer the needs of regional review; selected elements of the present lot may later be interpolated, on the basis of system, in sets which the author and publisher plan to provide. In preparing the several sequences, the same specimen was used, as far as possible, for the successive dissections in each series—to give a unity that otherwise would be lacking. Relations are presented exactly as they existed in the parts dissected.

The views comprising Section 4 visualize the thoracic wall, the thoracic viscera, and, to some extent, the structure of the back. Neighboring parts of the neck, the upper limb, and the abdominal wall

[7] FUNCTIONAL BRACING OF THE UPPER EXTREMITIES. Written and illustrated by Miles H. Anderson, Ed.D. Edited by Raymond E. Sollars. 463 pages, illustrated. $9.50. Springfield, Ill.: Charles C Thomas, 1958.

[8] A SYMPOSIUM ON NON-TOXAEMIC HYPERTENSION IN PREGNANCY. Edited by Norman F. Morris, M.C., M.B., B.S., M.R.C.O.G., and J. C. McClure Browne, B.Sc., M.B., B.S., F.R.C.S. (Edin.), F.R.C.O.G. 243 pages, 78 illustrations. $8.50. London: J. & A. Churchill Ltd.; Boston: Little, Brown & Co., 1958.

[9] A METHOD OF ANATOMY; DESCRIPTIVE AND DEDUCTIVE. By J. C. Boileau Grant, M.C., M.B., Ch.B., F.R.C.S. (Edin.). 6th ed. 879 pages, 862 illustrations. $11.00. Baltimore: Williams & Wilkins Co., 1958.

[10] A STEREOSCOPIC ATLAS OF HUMAN ANATOMY. By David L. Bassett, M.D. Section IV—The Thorax. View-MasterReels 113–122, 123–132. Color photographs by William B. Gruber. Portland: Sawyer's Inc., 1958.

have been included where necessary for reasons of topographic relationship. A more comprehensive study of the back is the subject of a separate section of the *Atlas*.

As customary in previous sections, the osteologic material is presented first. Then sequence of dissections is initiated with the exploration of the anterior and lateral parts of the chest wall, including the breast. Following this are several views of the thoracic viscera in situ. Detailed pictures of dissections of isolated hearts appear next in order; then the lungs are illustrated, both as isolated whole organs and in a series of dissections of the bronchial and vascular structures of the various lobes in situ.

The mediastinum and its contents, exclusive of the pericardium and heart, are the subjects of the subsequent group of dissections. Views of the mediastinum extend to paravertebral structures (the sympathetic trunks, the azygos and hemiazygos veins, the intercostal arteries, and regional lymphatic structures). Dissections of the diaphragm are pictured next in order.

The thorax is approached from the posterior aspect in the concluding series of dissections. Illustrative views of dorsal musculature, vertebral articulations, spinal cord, and the origins of spinal nerves in the thoracic region are included. Posterior views of the pleura and the relations of the thoracic viscera complete the section.

This ambitious atlas consits of three-dimensional kodachrome transparencies in full color, on 19 reels. The reels are stored protectively in numbered slots in the front of the volume. A table of contents, like that of a textbook, lists the title of each view, and the features illustrated in each. The reels are accompanied by text which presents pertinent information and drawings—each of the latter being fully labeled—provided with a scale of dimensions and suitable description.

The reels of pictures are to be studied with Sawyer's View-Master stereoscope. In addition to being usable by the individual, the pictures may be projected on a screen for instruction of classes and seminars in school, hospital, or clinical meeting.

Bassett's experience as a teacher, and his exceptional ability as a critical anatomist, would guarantee the quality of this set. He is most fortunate in having the willing counsel and guidance of equally distinguished colleagues, as well as the technical collaboration, in the capacity of photographer, of William B. Gruber. The skill of Mr. Gruber is as essential to such an endeavor as that of an artist is to the preparation of a textbook or atlas of the more familiar kind.

—Barry J. Anson.

THE BOOK, *Progress in Radiation Therapy*,[11] is the first of a series to appear at intervals of 1 to 2 years. Franz Buschke has assumed the editorial responsibility for these publications. The editorial policy as stated in the introduction is not to present digests or abstracts but rather to provide comprehensive critical reviews of fundamental biologic, physical, or clinical problems having immediate application to clinical radiation therapy. To accomplish this type of presentation particular phases of the subject will be discussed by authors who have had extensive personal experience in a specific area.

In keeping with the policy, 13 authors have contributed chapters in the first volume in the series. Following the introduction by the Editor, the first 2 chapters are devoted to a discussion of the history of clinical radiation therapy by James T. Case and the history of radiation sources by E. Dale Trout. In the subsequent chapters, the subject matter discussed includes biologic, physical, and clinical problems in approximately equal proportion with a final contribution by R. R. Newell on radiation therapy as a medical specialty.

In reading this book one is impressed by the tremendous advances in the field of radiation therapy during the past one-half century but much still remains to be done. Publications such as this volume may well serve to stimulate further investigators and clinicians and to bring about continued progress in clinical radiation therapy. The editorial policy and concept of the editor and publisher in the treatment of the subject are commendable. This and future volumes will be most useful in the training of young men and will serve to complement information obtainable in current journals. In future presentations it is hoped that the clinical aspects will receive major but not disproportionate emphasis, as true progress is best measured by the benefit to the sick patient.

This book represents an authoritative contribution in the field of radiation therapy and is recommended without reservation not only to radiologists but to any physician or investigator in this field. It will also be invaluable as a reference to be used in residency working training programs.

—Earl E. Barth.

THE THIRD EDITION of Stallard's *Eye Surgery*[12] continues the comfortable format that characterized the previous two editions. In this day of quarto-sized texts weighing upward of 7 pounds, Stallard's book has always been a delight to the resident in ophthalmology. It has been small enough to be surreptitiously consulted and light enough to be carried into postprandial seclusion for a spot of quiet reading.

However, this new edition is some 230 pages longer than the second, and the number of illustrations has been increased some 20 per cent. These are still largely drawings done by the author himself. This is in keeping with the personal feeling of the text. It remains largely the recommendations of one surgeon rather than a compendium of surgical procedures. In keeping with the tenor of the times, the section on war injuries has been curtailed and the section on corneal transplants enlarged. There has also been added a brief section on the use of acrylic implants in the anterior and posterior chamber in cataract surgery.

All in all, "Stallard" continues to be a worthwhile textbook of ophthalmic surgery and is highly recom-

[11]PROGRESS IN RADIATION THERAPY. Edited by Franz Buschke, M.D. with 13 contributors. 284 pages, illustrated. $9.75. New York and London: Grune & Stratton, 1958.

[12]EYE SURGERY. By H. B. Stallard, M.B.E., M.A., M.D.(Cantab.), F.R.C.S.(Eng.). 3rd ed. 899 pages, 671 illustrations. $18.00. Baltimore: Williams & Wilkins Co., 1958.

mended to all oculists be they novices or *combattants anciens*.

—*David Shoch.*

IN THE BOOK *Notes de techniques chirurgicales de La Presse Medicale*,[13] with the help of a large number of outlines, a series of new and modified classical surgical techniques is explained. It presents a picture of up-to-date French surgery. The names of most of the authors are well known in Europe.

The book is subdivided into 6 chapters: (1) "Generalities," with emphasis on closure of wounds; (2) "Thorax and Rachis," surgery of the esophagus, heart, lungs, and dorsal spine; (3) "Abdomen," a very interesting chapter in which the new concepts of surgery of the stomach and intestine are discussed; (4) "Pelvis"; (5) "Urinary System," nephropexy, cervicocystopexy, and urethroplasty; (6) "Limbs," in which are discussed new techniques on recurrent luxation of the shoulder joint, paralysis of the deltoid muscle, reconstruction of the thumb, amputation of the fingers, construction of a bone bloc and arthrodesis of the hip, osteoarthritis of the knee, and surgical treatment of dilated veins.

This volume has two important advantages: It explains surgical problems which are met in daily surgical practice. Every surgeon will certainly find it of interest. Secondly, when time fails to carry out extensive reading, this book gives a summary of surgical techniques without long discussion. It is a book for the week end.

—*R. Van Riet.*

IN THESE DAYS of systems engineering and interdisciplinary committees, radiation biology and medicine stand out as a field embracing genetics, radiation physics, radiotherapy, nuclear chemistry, and a variety of related physical, chemical, and biologic specialties, each a worthy discipline in its own right. To the serious scholar or to the casual reader seeking orientation in this field, the volume *Radiation Biology and Medicine*[14] edited by Walter D. Claus of the Atomic Energy Committee provides a lucid and stimulating introduction.

The 33 carefully chosen chapters, each by a well known authority in his field, have been written in a scholarly manner, not talking down to the lay public, but, at the same time, avoiding the sophistication of the specialist talking to his colleagues, so that a most readable, authoritative, and well documented presentation is achieved.

This is a most timely report in view of the widespread and somewhat hysterical publicity concerning radiation effect, fall-out, etc., and should provide the thinking reader with a substantial scientific background for judgment on these questions on the basis of the scientific knowledge and theory existing today.

—*Paul V. Harper.*

THE EDITORS have succeeded in their original intent, namely, to provide a readily accessible volume for the busy resident surgeon so that he may reflect upon the accomplishments of his predecessors. To accomplish this goal the Editors have accumulated some of the original papers of 28 surgeons of the past and present, all of whom have contributed to the advancement of the art and science of surgery. There can be no doubt that the work of most of these men has long since attained its rightful place in surgical history. It is fitting that their most important articles should be grouped together in one volume, *Milestones in Modern Surgery*,[15] for those of us whose interests are primarily surgical.

The articles selected by the Editors to signify the *Milestones in Surgery* were chosen with certain criteria in mind. These were: (1) The article must present a significant advance in surgery; (2) it must demonstrate the scientific method; and (3) the principle or method described should still be of current value. In certain sections in the volume the last criterion can be questioned. To state that an article is of current practical value because it is of historical value may perhaps prove a point by default.

Each of the 28 papers in this volume is preceded by a short biographic sketch and a portrait of the author. The preliminary remarks are of interest, as are the comments from the Editors on a variety of subjects and thoughts. The Editors have thoughtfully included a section entitled "Milestones on the Horizon" which contains discussions regarding tissue transplantation and the new horizons that successful open-heart procedures have opened to the field of surgery.

No one can deny that the volume fills a void which has long existed. Only the true student of the history of medicine and surgery would have had the time and energy during his surgical training to seek out the original articles which first outlined the principles that he is now using in the operating room. The gap in this type of surgical knowledge has long been apparent and Drs. Hurwitz and Degenshein have done something to close it. No valid complaints can be made, either about the "milestones" included in this volume or the manner in which the volume has been assembled. This reviewer can well visualize the value that this book will have in his surgical library as a reference to the works of the great surgeons of the past and present. It would be even more valuable if, at the time of the first revision of the volume, the preliminary remarks prior to each article and the personal nature of the men contributing these works could perhaps be elaborated upon to a greater extent.

—*Orville F. Grimes.*

[13] NOTES DE TECHNIQUES CHIRURGICALES DE LA PRESSE MEDICALE. Collected by Lucien Leger. 318 pages, 209 illustrations. 3,800 fr. Paris: Masson et Cie, 1958.

[14] RADIATION BIOLOGY AND MEDICINE; SELECTED REVIEWS IN THE LIFE SCIENCES. Edited by Walter D. Claus. Prepared for the United States Atomic Energy Commission. 944 pages, illustrated. $11.50. Reading, Massachusetts: Addison-Wesley Publishing Co., Inc., 1958.

[15] MILESTONES IN MODERN SURGERY. By Alfred Hurwitz, M.D., and George A. Degenshein, M.D. 520 pages, illustrated. $15.00. New York: Paul B. Hoeber, Inc., 1958.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

ESSENTIALS OF GYNECOLOGY. E. Stewart Taylor, M.D. 502 pages, 343 illustrations. $12.00. Philadelphia: Lea & Febiger, 1958.

FRACTURES AND OTHER INJURIES. Edited by Edwin F. Cave, M.D. 863 pages, 612 illustrations. Chicago: The Year Book Publishers, 1958.

AGRESSOLOGIE. Cycle de conferences de l'année 1958, a l'École d'Application du Services de Santé Militaire du Val-de-Grâce. 257 pages, illustrated. 2.000 fr. Paris: Service de Propagande Edition, Information, 1958.

A DOCTOR SPEAKS HIS MIND. By Roger I. Lee, M.D. 120 pages. $3.00. Boston and Toronto: Little, Brown & Co., 1958.

A DISPOSICAO VASCULAR DA SUBMUCOSA DO ESTOMAGO; CONTRIBUICAO PARA O ESTUDO DAS ALTERACOES VASCULARES NA ULCERA GASTRICA; DISSERTACAO DE CANDIDATURA AO GRAU DE DOUTOR APRESENTADA A FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO. By Manuel Teixeira Amarante, Jr. 149 pages, 38 illustrations. Porto: Imprensa Portuguesa, 1958.

THIRD TISSUE HOMOTRANSPLANTATION CONFERENCE. Consulting Editor Blair O. Rogers. (Annals of the New York Academy of Sciences. Vol. 73, Art. 3. Pages 539–868.) $5.00. New York: The New York Academy of Sciences, 1958.

CONTRIBUTIONS OF THE PHYSICAL, BIOLOGICAL, AND PSYCHOLOGICAL SCIENCES IN HUMAN DISABILITY. Consulting Editor Renato Contini. (Annals of the New York Academy of Sciences. Vol. 74. Art. 1. Pages 1–160.) $3.50. New York: The New York Academy of Sciences, 1958.

ENZYMES IN BLOOD. Consulting Editor Laurens P. White. (Annals of the New York Academy of Sciences. Vol. 75, Art. 1. Pages 1–384.) $5.00. New York: The New York Academy of Sciences, 1958.

THE BASIC AND CLINICAL RESEARCH OF THE NEW ANTIBIOTIC, KANAMYCIN. Consulting Editor Maxwell Finland. (Annals of the New York Academy of Sciences. Vol. 76, Art. 2. Pages 17–408.) $5.00. New York: The New York Academy of Sciences, 1958.

GENETIC CONCEPT FOR THE ORIGIN OF CANCER. Consulting Editor Leonell C. Strong. (Annals of the New York Academy of Sciences. Vol. 71, Art. 6. Pages 807–1241.) $5.00. New York: The New York Academy of Sciences, 1958.

SURGICAL CONVALESCENCE. Consulting Editor F. Curtis Dohan. (Annals of the New York Academy of Sciences. Vol. 73, Art. 2. Pages 381–538.) $4.00. New York: The New York Academy of Sciences, 1958.

THIRD TISSUE HOMOTRANSPLANTATION CONFERENCE. Consulting Editor Blair O. Rogers. (Annals of the New York Academy of Sciences. Vol. 73, Art. 3. Pages 539–868.) $5.00. New York: The New York Academy of Sciences, 1958.

CONTRIBUTIONS OF THE PHYSICAL, BIOLOGICAL, AND PSYCHOLOGICAL SCIENCES IN HUMAN DISABILITY. Consulting Editor Renato Contini. (Annals of the New York Academy of Sciences. Vol. 74, Art. 1. Pages 1–160.) $3.50. New York: The New York Academy of Sciences, 1958.

CLINICAL NEUROSURGERY. Proceedings of the Congress of Neurological Surgeons, Washington, D. C., 1957. 206 pages, illustrated. $8.00. Baltimore: Williams & Wilkins Co., 1958.

TEXTBOOK OF SURGERY. Edited by Guy Blackburn, M.B.E., M.Chir., F.R.C.S., and Rex Lawrie, M.D., M.S., F.R.C.S., M.R.C.P. Foreword by Sir Russell Brock, M.S., F.R.C.S., F.A.C.S.(Hon.). 1122 pages, illustrated. $16.75. Springfield, Ill.: Charles C Thomas, 1958.

REVERSIBLE RENAL INSUFFICIENCY; DIAGNOSIS AND TREATMENT. By Donald H. Atlas, M.D., Ph.D., F.A.C.P., and Peter Gaberman, M.D. 233 pages, 19 illustrations. $7.00. Baltimore: Williams & Wilkins Co., 1958.

ESSAYS IN EPONYMY. OBSTETRIC AND GYNECOLOGIC MILESTONES. By Harold Speert, M.D. 700 pages, illustrated. $15.00. New York: The Macmillan Co., 1958.

AUS SPEZIELLEN ELEKTROBIOLOGISCHEN KLAREFFEKTEN ABGELEITETE UNIVERSALERE PERSPEKTIVEN. By Dipl.-Ing. G. Neidl. 31 pages, 8 illustrations. Westberlin: Theodor Hoelscher, 1958.

SURFACE AND RADIOLOGICAL ANATOMY; FOR STUDENTS AND GENERAL PRACTITIONERS. By A. B. Appleton, W. J. Hamilton, and Ivan C. C. Tchaperoff. 4th ed. By W. J. Hamilton, M.D., and G. Simon, M.D. 355 pages, 416 illustrations. $9.50. Baltimore: The Williams & Wilkins Co., 1958.

LES TRAUMATISMES DU THORAX; THÉRAPEUTIQUE PRATIQUE PRÉVENTION DES SÉQUELLES.-EXPERTISES. By Jean-Charles Sournia. Preface by P. Santy. 354 pages, illustrated. 4,800 fr. Paris: G. Doin & Cie, 1958.

NOUVELLE PRATIQUE CHIRURGICALE ILLUSTRÉE. By Jean Quénu. Fascicule 12. 296 pages, 254 illustrations. 3,500 fr. Paris: G. Doin & Cie, 1958.

CLINICAL OBSTETRICS AND GYNECOLOGY. Vol. I. No. 4. Operative Obstetrics. Edited by J. Robert Willson, M.D., and Genital Cancer. Edited by Daniel G. Morton, M.D. 281 pages, illustrated. New York: Paul B. Hoeber, Inc., 1958.

KLINISCHE METHODEN DER BLUTGERINNUNGSANALYSE. By Prof. Dr. J. Jürgens, and Doz. Dr. F. K. Beller. Foreword by Prof. Dr. M. Gänsslen. 392 pages, 104 illustrations. $13.35. Stuttgart: Georg Thieme Verlag, 1958.

II CONGRESSO LUSO-ESPANHOL DE CIRURGIA ORTOPÉDICA E TRAUMATOLÓGICA. TRAUMATISMOS VERTEBROMEDULARES CERVICAIS COM PERTURBAÇÕES NERVOSAS. By A. Ferreira Alves and Corino Andrade. 109 pages, 50 illustrations. Porto, Portugal, 1958.

SCHMERZLOSE GEBURT DURCH PSYCHOPROPHYLAXE. By Dr. F. Roth. Foreword by Prof. Dr. W. Neuweiler. 124 pages, 8 illustrations. $2.85. Stuttgart: Georg Thieme Verlag, 1958.

DIE PRÄNATALEN INFEKTIONEN DES MENSCHEN; UNTER BESONDERER BERUECKSICHTIGUNG VON PATHOGENESE UND IMMUNOLOGIE. By Dr. Heinz Flamm. Foreword by Prof. Dr. Richard Bieling. 135 pages, 2 illustrations. $4.20. Stuttgart: Georg Thieme Verlag, 1958.

ACTAS DE LA ASOCIACION ARGENTINA DE CIRUGIA. VIGESIMONOVENO CONGRESO ARGENTINO DE CIRUGIA. Fascículo I. Benos Aires: Secretaria de la Asociacion, 1958.

CHRONIC SUBDURAL HEMATOMA; WITH PARTICULAR REFERENCE TO THE DIAGNOSIS; A CLINICAL, ROENTGENOLOGICAL AND ELECTROENCEPHALOGRAPHICAL STUDY. By Ragnar Nordlie. 164 pages, illustrated. Oslo, Norway: Johan Grundt Tanum Forlag, 1958.

TREATMENT OF CANCER AND ALLIED DISEASES; TUMORS OF THE NERVOUS SYSTEM. Edited by George T. Pack, M.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S. 2nd ed., vol. II. 316 pages, 340 illustrations. $15.00. New York: Paul B. Hoeber, Inc., 1959.